

Fig. 1

1 MTSIMLLLLFAFVQPCASIVEKRCGPIDIRNRPWDIKPQWSKLGDPNEKDLAQRMVNCT
 61 VVEGSLTISFVLKHKTKAQEEMHRSLOPRYSQDEFITFPHLREITGTLVLFETEGLVDLR
 121 KIFPNLRVIGGRSLIQHYALIIYRNPDL EIGLDKLSVIRNGGVRIIDNRKLCYTKTIDWK
 181 HLITSSINDVVVDNAAEYAVTETGLMCPRGACEEDKGESKCHYLEEKNQEQGVERVQSCW
 241 SNTTCQKSCAYDRLLPTKEIGPGCDANGDRCHDQCVGGCERVNDATAACHACKNVYHKGKC
 301 IEKCDALYLLQRRCVTREQCLQNPVLSNKTVP IKATAGLCSDKCPDGYQINPDDHRE
 361 CRKCVGKCEIVCEINHVIDTFPKAQAIRLCNIIDGNLTIEIRGKQDSGMASELKDIFANI
 421 HTITGYLLVRQSSPFISLNMFRNLRRIEAKSLFRNLYAITVFENPNLKKLFDSTDTLTD
 481 RGTVSIANNKMLCFKYIKQLMSKLNIPLDPIDQSEGTNGEKAICEDMAINVSITAVNADS
 541 VFFSWPSFNITDIDQRKFLGYELFFKEVPRIDENMTIEEDRSACVDSWQSVFKQYYETSN
 601 GEPTPDIFMDIGPRERIRPNTLYAYYVATQMV LHAGAKNGVSKIGFVRTSYYPDPPTLA
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 721 KETIVADKPVDIPSSRTVAPTLLTMMGHEDQQKTCAATPGCCSCSAIEESSEQNKKKRPD
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 841 IHISKKKPSSSSTTSTPAPTIASMYALTRKPTTVPGTIRIRLYEIIYEPLPGSWAINVSALA
 901 LDNSYVIRNLKHYTLYAISLSACQNMTVPGASCSISHRAGALKRTHITDIDKVLNETIE
 961 WRFMNNSQQVNVTWDPPTTEVNGGIFGYVVKLKS KVDGSI VMTRCVGAKRGYSTRNQGVLF
 1021 QNLADGRYFVSVTATSVHGAGPEAESSDPIVVMTPGFFTVEIILGMLLVFLILMSIAGCI
 1081 IYYYYIQVRYGKKVKALSDFMQLNPEQCVDNKYNADDWELRQDDVVLGQQCGEGSFGKVYL
 1141 GTGNVVSLSMGRDFGPCAIKINVDDPASTENLNYLMEANIMKNFKTNFIVQLYGVISTVQ
 1201 PAMVVMEMMDLGNLRDYLRSKREDEVFNEDCNFFDIIPRDKFHEWAAQICDGMAYLESL
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 1381 WRYSRDRPTFLQLVHLIAAEASPEFRDLSFVLTDNQMI LDDSEALDLDIDDDTMDNDQV
 1441 VEVAPDVENVEVQSDSERRNTDSIPLKQFKTIPPINATTSHSTISIDETPMKAKQREGSL
 1501 DEEYALMNHSGGPSDAEVRTYAGDGDYVERDVRENDVPTRRNTGASTSSYTGGGPYCLTN
 1561 RGGSNERGAGFGEAVRLTDGVGSGHLNDDDYVEKEISSMDTRRSTGASSSSYGVPTNWS
 1621 GNRGATYYT SKAQQAATAAAAAAALQQQQNGGRGDRLTQLPGTGHLQSTRGGQDGDYIE
 1681 TEPKNYRNNGSPSRNGNSRDIFNGRSAFGENEHLIEDNEHHPLV

Fig. 2A

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Fig. 2B (sheet 1 of 3)

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Fig. 2B (sheet 2 of 3)

5551 atggatctcc atcgcgaaac ggcaacagcc gtgacatttt caacggacgt
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Fig. 2B (sheet 3 of 3)

IGF-IR RGAIRIEKNADLCYLSFTWDMSLTDAYSNNYIVGNKPKK..ECG.DLCPTWEZEKPMCEKTTINNEYNYR.....CWTNRCQKMC.....PSTC
InR RGSVRIEKNNECYLATIDWSRHDSDVEDNYIVLNKDDNE.ECG.DICPPTAKGKTNCPTATVINGQFVER.....CWTSHCQKVC.....PTIC
DInR RGVRIEKNHKLCTDRTIDWLEHDAENESQLVLTENGKEKESLSKCPGEIRIEEGHDNTALEGNLASCQLHNRRRLCWN SKLCQTKC.....PEKC
DAP-2 NCGVRIIDNRKLCCTKTIDWKLHLTSSINDVVDNAEYAVTETGLMCERGACEEDKGESKCHYLEEKNZQGVVERVQSCWNTTTCQSCAYDRLLPTKE

IGF-IR GKRACTENNECCHPEGLGSC.SAPDNDTACVACRHHYYAGCVCPACPPNTVREEGWRCVDRDFCAM²L.....SAESSDSEGFVIHDGECMQEQECPSPGSGIIRN
 InR KSHGCTAAGLCCHSEGLGNC.SQDDPTKCVACRNFYLDGRCVETCCPPYVHEQDWRGVNFSCQDTHHKCKNRRRQGCQHYVIHNNKCIPEPCPSGYTMN
 DinR .RNNCIDETHCCSQDGLGCVIDKNGNESICISCRNVSPNNICMDSCEKGYQF.DSRCVTANEICITITKFTETNSVYSG...IPYNGQCITHCPTGY.QK
 DAF-2 IGPGCDANGDRCHDQGVGGC.ERVNDATACHACKNVYHKGKCIKCDADHL²EQLRRCVTRREQQLQENPVLNKTVP...IKATAGLCSDDKCPDGLQIN
 R ↑ P ↑ L (mg43)
 R Y (mg43) vS (sa187)

IGF-IR GSQSMYCIPEGCPCKPVCEEKKKTKTIDSVTSQAWLQCGCTIFKGN..LLINIRR..GNNIASLEENFMGLTEVTCYVKIRHSHALVLSLSEKKNRLRLILG
Inr SSN.LLCTPCLGPCPKVCHLLEGEXTIDSVTSQALRGCTVINGS..LLINIRG..GNNLAAETLANGLTEETSCTYKIRRSYALVLSLSEFFKRLRLIRG
Dinr SENKRMCEPCPG...KCDKECSGLIDSLERAREFHGCTIITCTEPTSTIKRESCAHVMDLKYGLAAVHKQSSIMVHLYTGLKSLKKEFQSLTEISG
DAF-2 PDDHRECRKCVKCEIVCEI...NHVIDFPPKAQAIRLCLNIIDGN..LLEIRGKQDSGMASELKIDIFANETHETGYLLVROSSPISLNMERNLRRIEA

IGF-IR EEQLEG⁺YSFYALD⁺ONTQLEWD⁺WDRN⁺TLKAG⁺KMY⁺AFNPK⁺IC⁺SELYRME⁺EVGT⁺KGR. QSKCD⁺INTRN⁺NGERAS⁺CESD⁺VLH⁺FTST⁺TSKN.....
Inr ETELE⁺NYSFYALD⁺ONTQLEWD⁺SKHN⁺TLTCK⁺LFFH⁺YFNPK⁺IC⁺SEH⁺KME⁺EVSG⁺TGKR. QERN⁺DALK⁺TNCD⁺QAS⁺ENEL⁺LKFS⁺YTSFD.....
Dinr DPEMD⁺ADKYALVLD⁺NRD⁺TLDEWG⁺PQOT⁺VEL⁺IRKG⁺VFH⁺FNPK⁺IC⁺SEH⁺QLP⁺MLASK⁺PKF⁺EGDS⁺GNR⁺SGCT⁺AVLNV⁺TLQSVG⁺ANSALN.....
DAF-2 KSLFR⁺NLYAIT⁺V⁺ANPN⁺EKK⁺LED⁺STDT⁺ELDR⁺GT⁺SVIAN⁺KML⁺CF⁺Y⁺ELQ⁺LM⁺SKLNIP....LDPI⁺QSEGT⁺NCKE⁺KA⁺ICED⁺MAN⁺V⁺ISIT⁺AVNADS.....

↑
L(e1368)T(e1365)
↑
N(sa229)

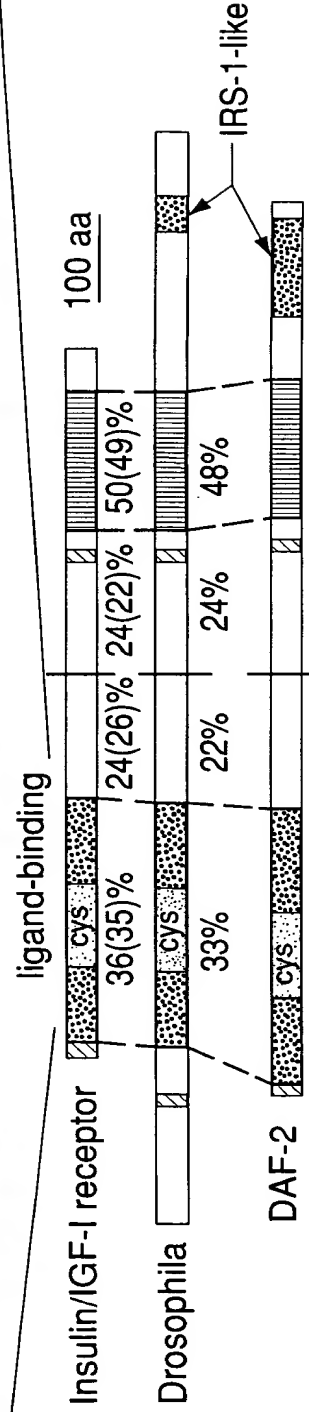


Fig. 2C (sheet 1 of 2)

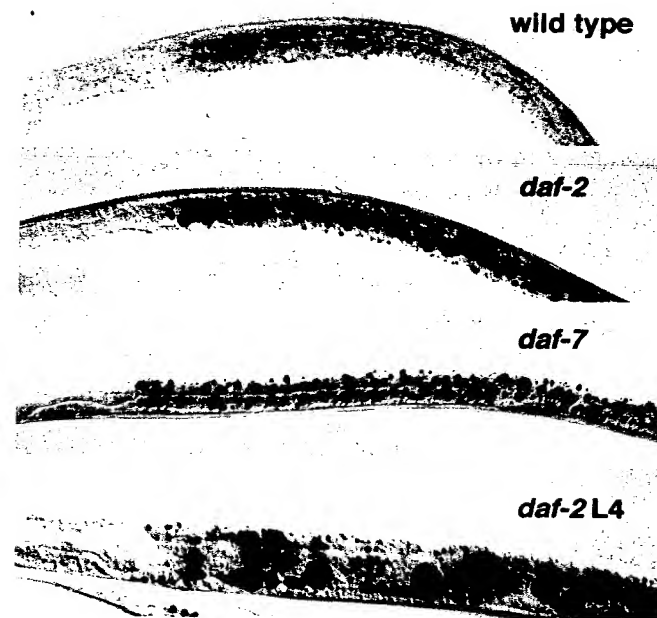


Fig. 3

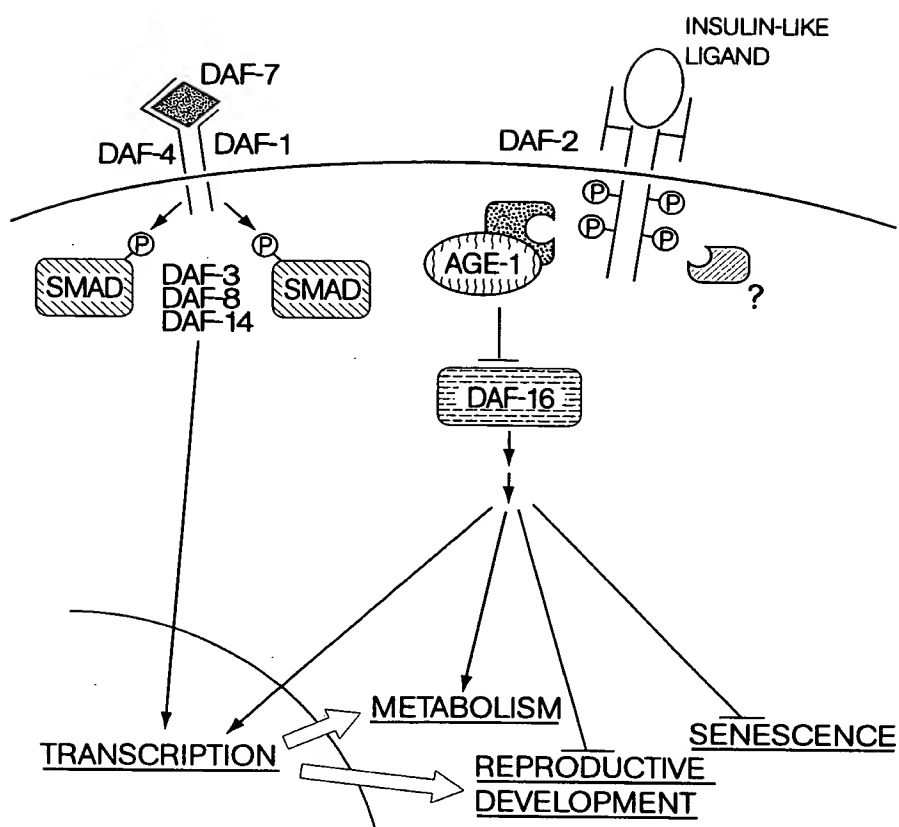


Fig. 4

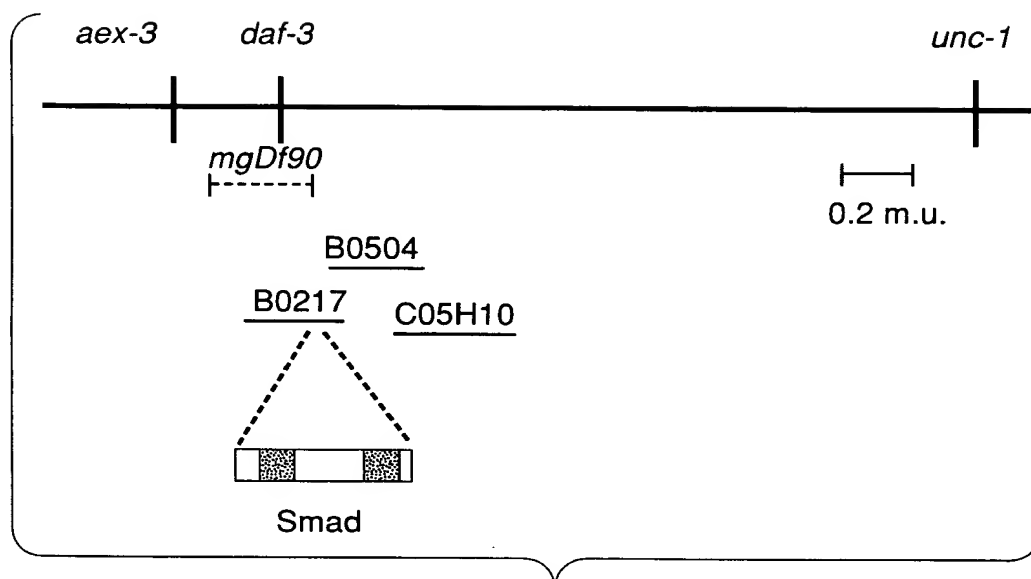


Fig. 5A

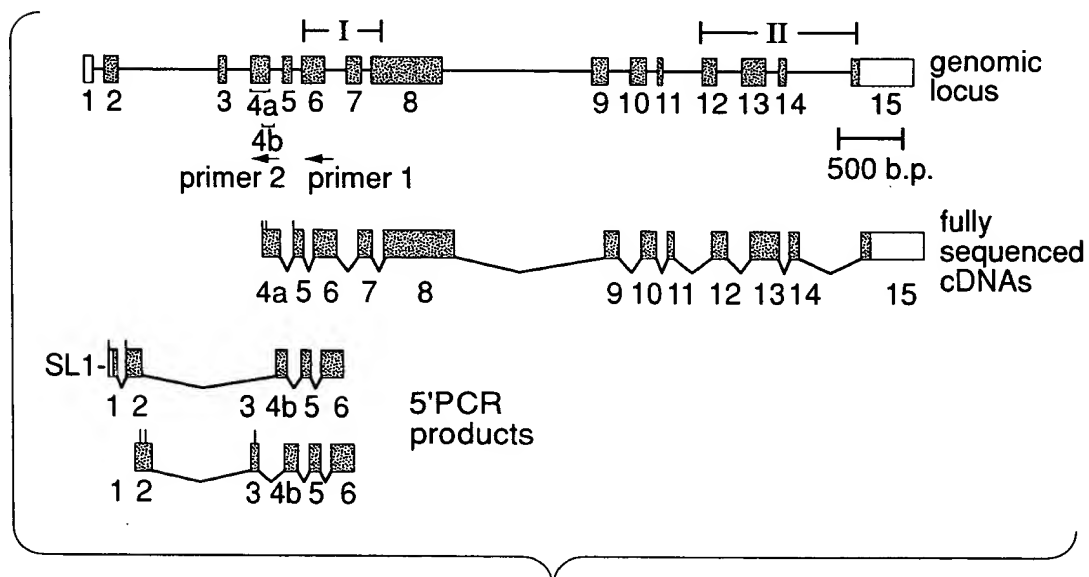


Fig. 5B

Domain I

DAF-3 .NIDREFDQKACESLVKKLKDKKNDLQNLIDVVL SKGTYTGCITIPRTL DG
 DPC4 GGESETFAKRAIESLVKKLKEKKDELDSLITAITTNGAHPSKCVTIQRTL DG
mg125 P->L
 RLQVHGRKGFPFHVYVYGLWRFNEMTKNETRHVDHCKHAFEMKSDMVCVNPYH
 RLQVAGRKGFPFHVYARLWRWPD LHKNELKHVKYCQYAFDLKCD SVCVNPYH

Domain II

DAF-3 IVYYEKNLQIGE..KKCSRGNFHVDGGFI..CSENRYSLGLEPNPIREPVAFKV
 DPC4 IAYFEMDVQVGETFKVPSSCPIVTVDGYVDPSSGDRFCLGQLSNVHRTEAIERA
mg132 G->E
 RKAIVDGI RFSYKKDGSVWLQNRMKYPVFVTS GYLDEQSGGLKKDKVHKVYGCA
 RLHIGKGVQLECKGEGDVWVRCLSDHAVFVQSY YLDREAGRAPGDAVHKIYPSA
 SIKTFGFNVSKQIIRDALLSKQMA....TMYLQ GKLT PMNYIYEKKTQEELRRE
 YIKVFDLRQCHRQMQQQAATAQAAAAAQA AAVAGNIPGPGSVGGIAP AISLSAA
 ATRTTDSLAKYCCVRVSFCKGFG EAYPERPSIHDCPVWIELKINIAYDFMD
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Fig. 5C



Fig. 6A

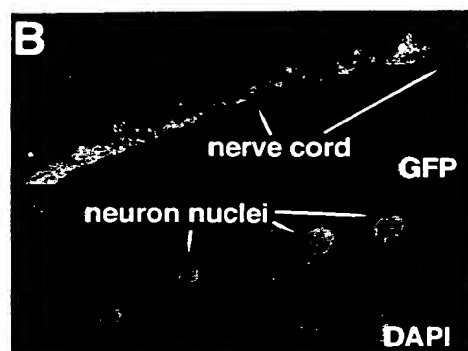


Fig. 6B

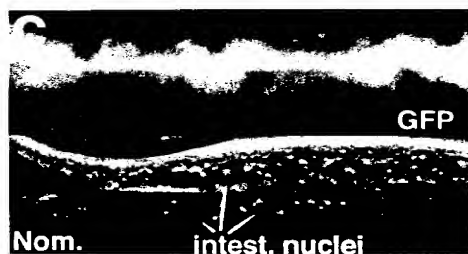


Fig. 6C

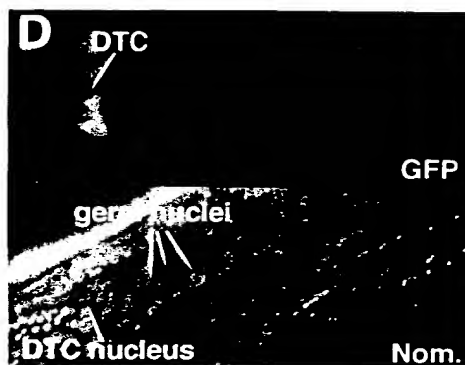


Fig. 6D



Fig. 6E

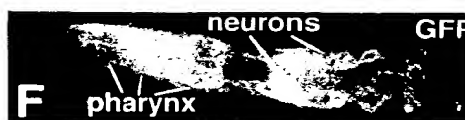


Fig. 6F



Fig. 6G

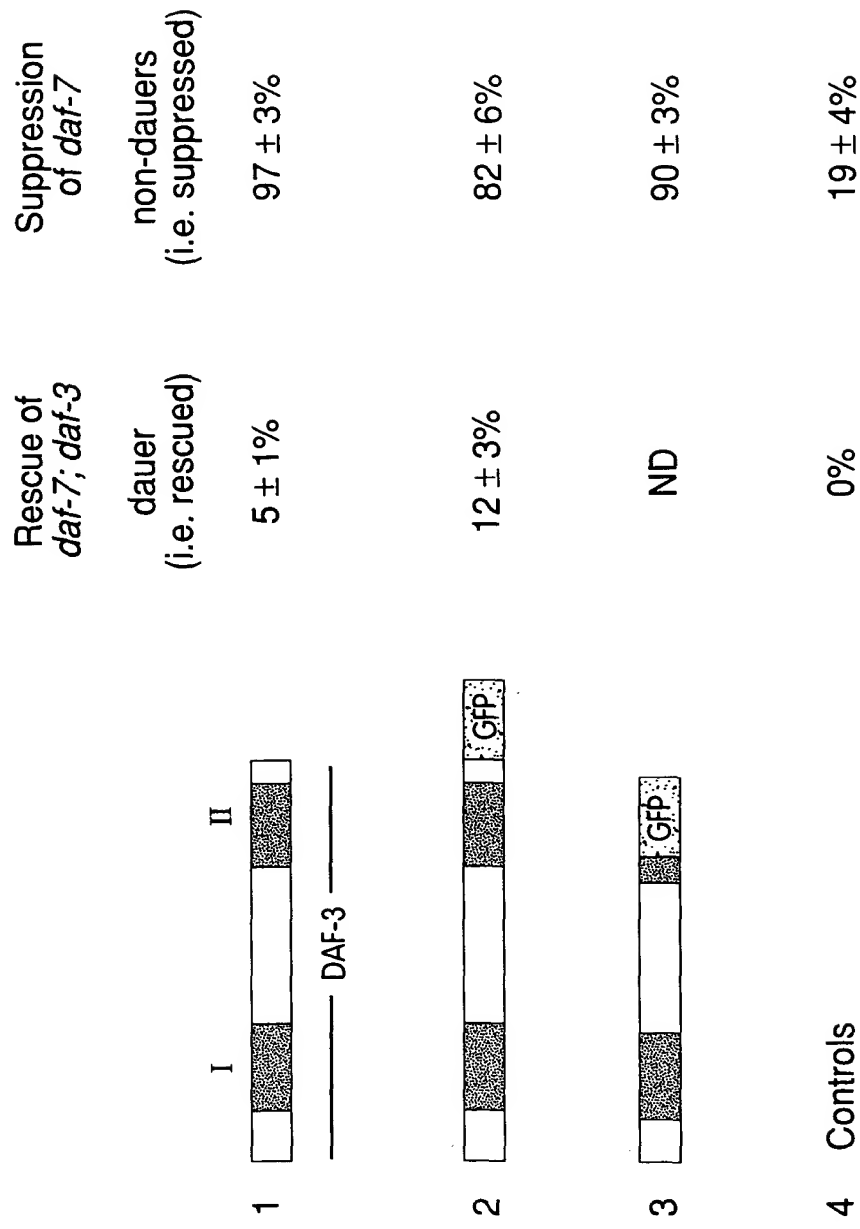


Fig. 7



Fig. 8A

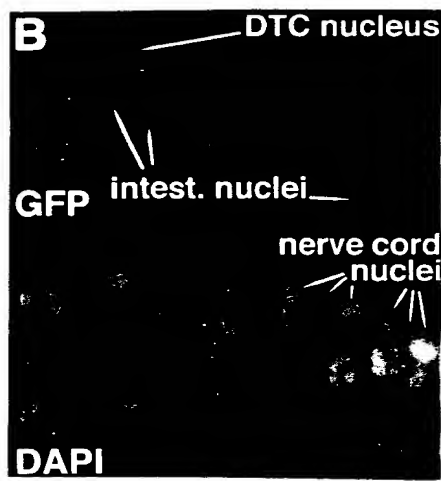


Fig. 8B

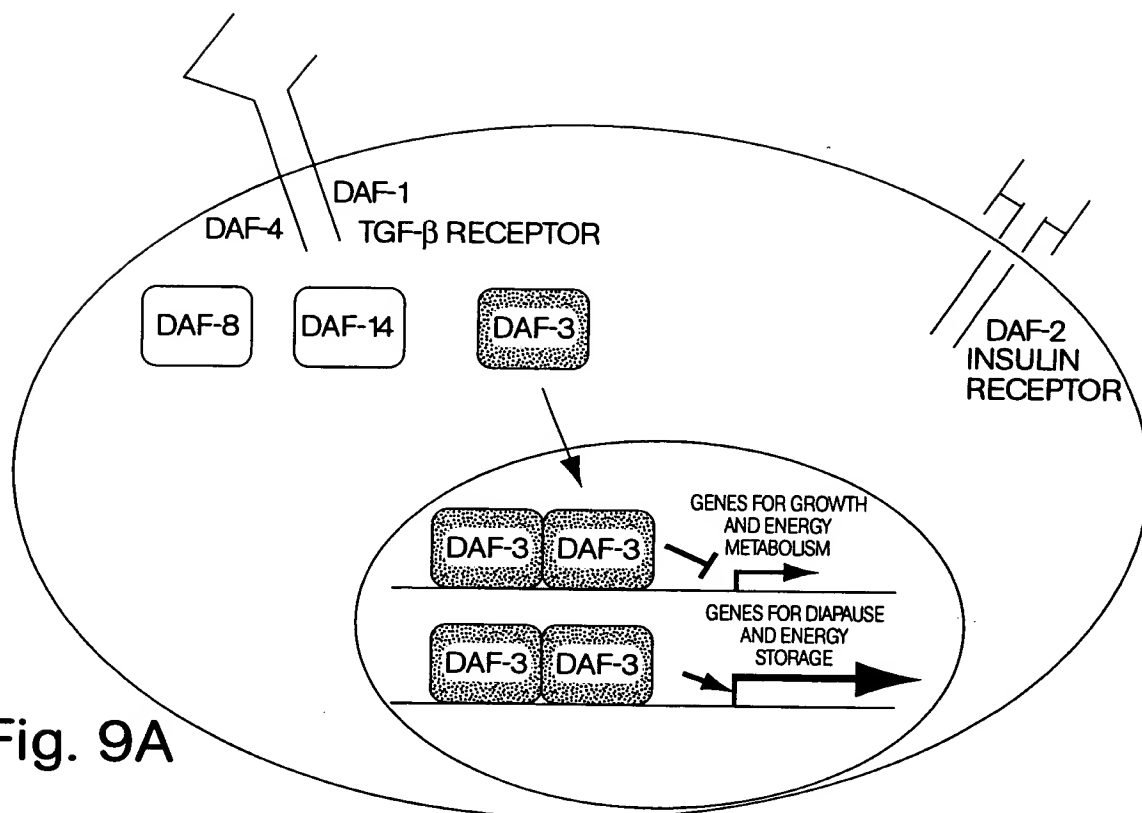


Fig. 9A

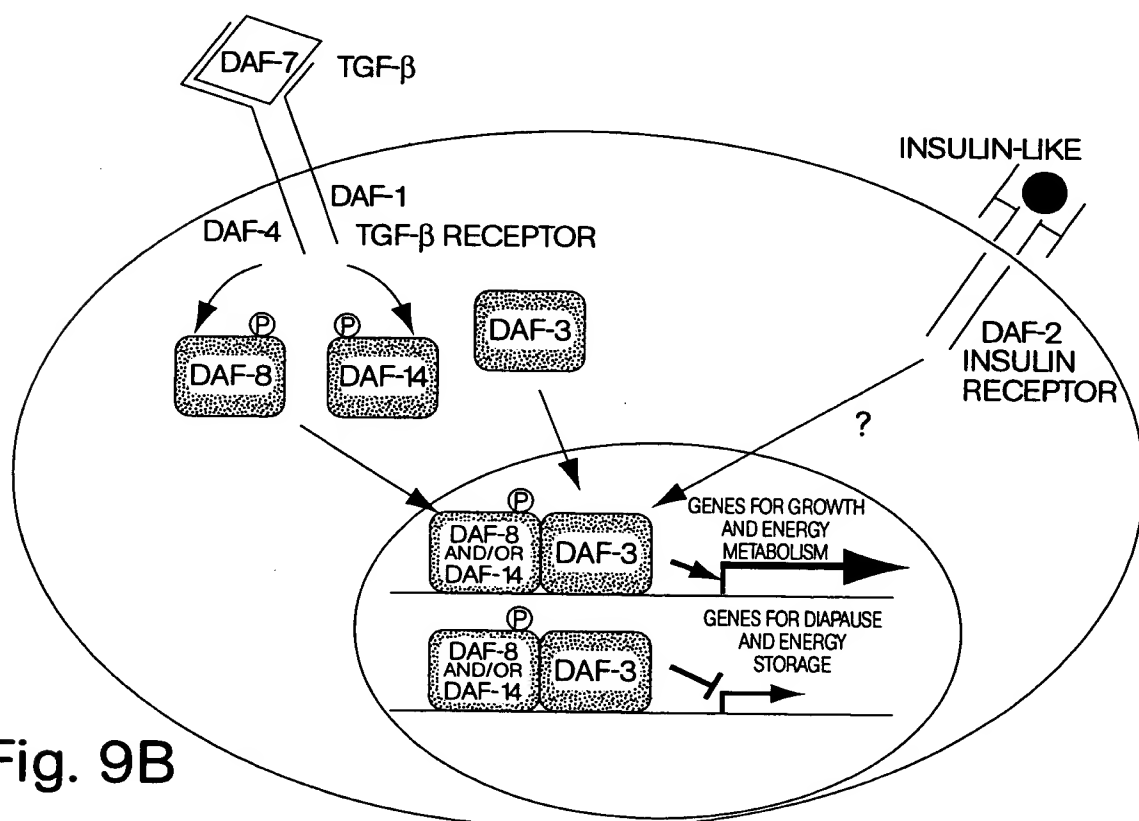


Fig. 9B

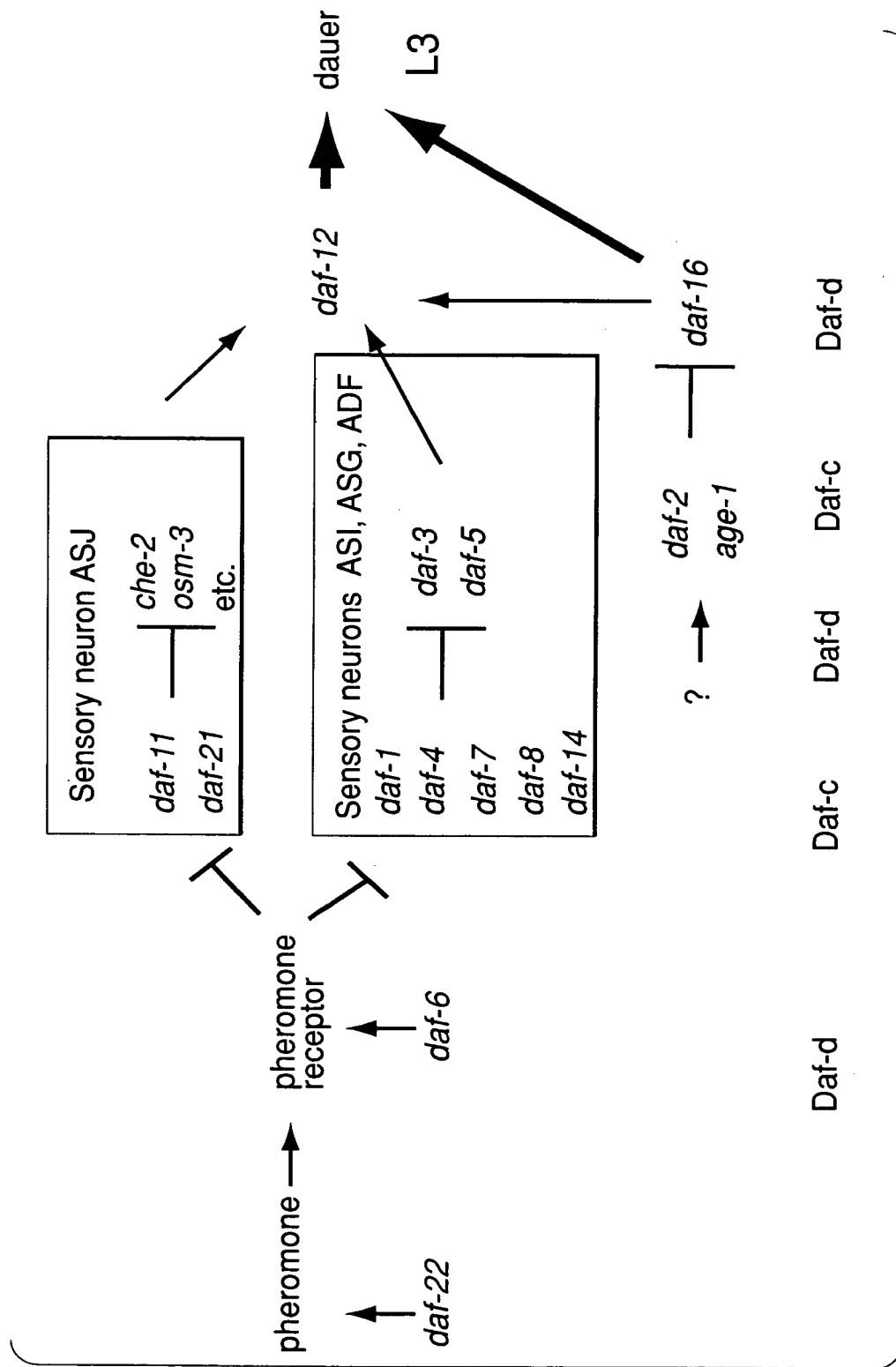


Fig. 10

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101	aatgggaaat	cccgccatat	ttggatccag	acagtcagga	tgatgacccg
151	gaagatggtg	tcaactaccc	ggatccagat	ttatttgaca	caaaaaacac
201	aatatgacc	gagtacgatt	tggatgtgtt	gaagcttgga	aaaccagcag
251	tagatgaagc	acggaaaaag	atcgaagtcc	ccgacgctag	tgcgccgcca
301	aacaaaattg	tagaatattt	gatgtattat	agaacgttaa	aagaaagtga
351	actcatacaa	ctgaatgcgt	atcggacaaa	acgaaatcga	ttatcgttga
401	acttgggtcaa	aaacaatatt	gatcgagagt	tcgaccaaaa	agcttgcgag
451	tccctgggtga	aaaaattgaa	ggataagaag	aatgatctcc	agaacctgat
501	tgatgtggtt	ctttcaaaaag	gtacaaaata	taccggttgc	attacaattc
551	caaggacact	tgatggccgg	ttacaggtcc	acggaagaaa	aggtttcctt
601	cacgtagtct	atggcaaact	gtggagggtt	aatgaaatga	caaaaaacga
651	aacgcgtcat	gtggaccact	gcaagcacgc	atttgaaatg	aaaagtgaca
701	tggtatgcgt	gaatccctat	cactacgaaa	ttgtcattgg	aactatgatt
751	gttgggcaga	gggatcatga	caatcgagat	atgccgccgc	cacatcaacg
801	ctaccacact	ccaggtcggc	aggatccagt	tgacgatatg	agtagattta
851	taccaccagc	ttccattcgt	ccgcctccga	tgaacatgca	cacaaggcct
901	cagcctatgc	ctcaacaatt	gccttcagtt	ggcgcaacgt	ttgcccattc
951	tctcccacat	caggcgccac	ataaccagg	ggtttcacat	ccgtactcca
1001	ttgctccaca	gacccattac	ccgttgaaca	tgaacccaat	tccgcaaatg
1051	ccgcaaatgc	cacaaatgcc	accacctctc	catcagggat	atggaatgaa
1101	tgggccgagt	tgctcttcag	aaaacaacaa	tccattccac	caaaatcacc
1151	attataatga	tattagccat	ccaaatcact	attcctacga	ctgtgggtccg
1201	aacttgtagc	ggtttccaac	tccttatccg	gattttcacc	atcctttcaa
1251	tcagcaacca	caccagccgc	cacaactatc	acaaaaccat	acgtcccaac
1301	aaggcagtc	tcaaccagg	caccaaggtc	aggtaccgaa	tgatccacca
1351	atctcaagac	cagtgttaca	accatcaaca	gtcaccttgg	acgtgttccg
1401	tcggtactgt	agacagacat	ttggaaatcg	atTTTTtgaa	ggagaaagtg
1451	aacaatccgg	cgcaataatt	cggcttagta	acaaattcat	tgaagaattt
1501	gattcgccga	tttgtggtgt	gacagttgtt	cgaccgcgga	tgacagacgg
1551	tgaggttttg	gagaacatca	tgccggaaga	tgcaccatat	catgacattt
1601	gcaagttcat	tttgaggctc	acatcagaaa	gtgtaacttt	ctcaggagag
1651	gggcccaga	ttagtgattt	gaacgaaaaa	tggggaacaa	ttgtgtacta
1701	tgagaaaaat	ttgcaaattg	gcgagaaaaa	atgttcgaga	ggaaatttcc
1751	acgtggatgg	cggattcatt	tgctctgaga	atcgttacag	tctcggactt
1801	gagccaaatc	caattagaga	accagtggcg	tttaaagtcc	gtaaagcaat
1851	agtggatgga	attcgctttt	cctacaaaaa	agacgggagt	gtttggcttc
1901	aaaaccgcat	gaagtaccgg	gtatttgtca	cttctgggta	tctcgacgag
1951	caatcaggag	gcctaaagaa	ggataaagtg	cacaaagttt	acggatgtgc
2001	gtctatcaaa	acgtttggct	tcaacgtttc	caaacaaatc	atcagagacg
2051	cgcttctttc	caagcaaatg	gcaacaatgt	acttgcaagg	aaaattgact

Fig. 11A (sheet 1 of 2)

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2101 cccgatgaatt atatctacga gaagaagact caggaagagc tgcgaaggga
2151 agcaacacgc accactgatt cattggccaa gtactgttgt gtccgtgtct
2201 cgttctgcaa aggatttgga gaagcatacc cagaacgccc gtcaattcat
2251 gattgtccag tttggattga gttgaaaatc aacattgcct acgatttcat
2301 ggattcaatc tgccagtaca taaccaactg cttcgagccg ctaggaatgg
2351 aagattttgc aaaattggga atcaacgtca gtgatgacta aatgataact
2401 tttttcactc accctactag atactgattt agtcttattc caaatcatcc
2451 aacgatatca aactttttcc tttgaacttt gcatactatg ttatcacaag
2501 ttccaagcag tttcaataca aacataggat atgttaacaa cttttgataa
2551 gaatcaagtt accaactggt cattgtgagc tttgagctgt atagaaggac
2601 aatgtatccc atacctcaat ctttaatagt catcagtcac tgggtcccgc
2651 ccaatttttt cgattcgcat atgtcatata ttgcaccgtg gcccttttta
2701 ttgtaacttt taatatattt tcttcccaac ttgtgaatat gattgatgaa
2751 ccaccatttt gagtaataaa tgtatttttt gtgg

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Fig. 11A (sheet 2 of 2)

1	gtaatcaaat	tgtaaaggaa	aatattaat	agtcagagta	cacataaatg
51	ggtgatcatc	ataatttaac	gggccttccc	ggtacctcca	tcccgccaca
101	gttcaactat	tctcagcccg	gtaccagcac	cggaggcccg	ctttatggtg
151	gaaaaccttc	tcatggattg	gaagatattc	ctgatgtaga	ggaatatgag
201	aggaacctgc	tcggggctgg	agcaggtttt	aatctgctca	atgtaggaaa
251	tatggctaata	gttcccgcag	agcacacacc	gatgatgtca	ccagtgaata
301	caactacaaa	gattctacaa	cggagtggta	ttaaaatgga	aatcccgccca
351	tatttggatc	cagacagtca	ggatgatgac	ccggaagatg	gtgtcaacta
401	cccggatcca	gatttatttg	acacaaaaaa	cacaaatatg	accgagtacg
451	atttggatgt	gttgaagctt	ggaaccag	cagtagatga	agcacggaaa
501	aagatcgaag	ttcccgcagc	tagtgcccg	ccaaacaaaa	ttgtagaata
551	tttgatgtat	tatagaacgt	taaaagaaag	tgaactcata	caactgaatg
601	cgtatcggac	aaaacgaaat	cgattatcgt	tgaacttggg	caaaaacaat
651	attgatcgag	agttcgacca	aaaagcttgc	gagtccctgg	tgaaaaaatt
701	gaaggataag	agaatgatc	tccagaacct	gattgatgtg	gttctttcaa
751	aaggtacaaa	atataccggt	tgcattacaa	ttccaaggac	acttgatggc
801	cggttacagg	tccacggaag	aaaaggtttc	cctcacgtag	tctatggcaa
851	actgtggagg	tttaatgaaa	tgacaaaaaa	cgaaacgcgt	catgtggacc
901	actgcaagca	cgcatttgaa	atgaaaagtg	acatgggtatg	cgtgaatccc
951	tatcactacg	aaattgtcat	tggaaactatg	attgttgggg	agagggatca
1001	tgacaatcga	gatatgccgc	cgccacatca	acgctaccac	actccaggtc
1051	ggcaggatcc	agttgacgat	atgagtagat	ttataccacc	agcttccatt
1101	cgtccgcctc	cgatgaacat	gcacacaagg	cctcagccta	tgcctcaaca
1151	attgccttca	gttggcgcaa	cgtttgccca	tcctctccca	catcaggcgc
1201	cacataaacc	aggggtttca	catccgtact	ccattgctcc	acagacccat
1251	taccggttga	acatgaacc	aattccgcaa	atgccgcaa	tgccacaaat
1301	gccaccacct	ctccatcagg	gatatggaat	gaatgggccg	agttgctctt
1351	cagaaaacaa	caatccattc	cacaaaatc	accattataa	tgatattagc
1401	catccaaatc	actattccta	cgactgtggt	ccgaacttgt	acgggtttcc
1451	aactccttat	ccggattttc	accatccttt	caatcagcaa	ccacaccagc
1501	cgccacaact	atcacaaaac	catacgtccc	aacaaggcag	tcatcaacca
1551	gggcaccaag	gtcagggtacc	gaatgatcca	ccaatttcaa	gaccagtgtt
1601	acaaccatca	acagtcacct	tggacgtgtt	ccgtcggtag	tgtagacaga
1651	catttggaag	tcgatttttt	gaaggagaaa	gtgaacaatc	cggcgcaata
1701	attcgggtcta	gtaacaaatt	cattgaagaa	tttgattcgc	cgatttgtgg
1751	tgtgacagtt	gttcgaccgc	ggatgacaga	cggtgaggtt	ttggagaaca
1801	tcatgccgga	agatgcacca	tatcatgaca	tttgcaagtt	cattttgagg
1851	ctcacatcag	aaagtgtaac	tttctcagga	gaggggcccag	aagttagtga
1901	tttgaacgaa	aaatggggaa	caattgtgta	ctatgagaaa	aatttgcaaa
1951	ttggcgagaa	aaaatgttcg	agaggaaatt	tccacgtgga	tggcggattc
2001	atttgctctg	agaatcgtaa	cagtctcgga	cttgagccaa	atccaattag
2051	agaaccagtg	gcgttttaaag	ttcgtaaagc	aatagtggat	ggaattcgcct

Fig. 11B (sheet 1 of 2)

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2101 tttcctacaa aaaagacggg agtgtttggc ttcaaaaccg catgaagtac
2151 ccggtatttg tcacttctgg gtatctcgac gagcaatcag gaggcctaaa
2201 gaaggataaa gtgcacaaag ttacaggatg tgcgtctatc aaaacgtttg
2251 gcttcaacgt ttccaaacaa atcatcagag acgcgcttct ttccaagcaa
2301 atggcaacaa tgtacttgca aggaaaattg actccgatga attatatcta
2351 cgagaagaag actcaggaag agctgcgaag ggaagcaaca cgcaccactg
2401 attcattggc caagtactgt tgtgtccgtg tctcgttctg caaaggattt
2451 ggagaagcat acccagaacg cccgtcaatt catgattgtc cagtttggat
2501 tgagttgaaa atcaacattg cctacgattt catggattca atctgccagt
2551 acataaccaa ctgcttcgag ccgctaggaa tggaagattt tgcaaaattg
2601 ggaatcaacg tcagtgatga ctaaatagata acttttttca ctcaccctac
2651 tagatactga ttagtctta ttccaaatca tccaacgata tcaaactttt
2701 tcctttgaac tttgcatact atgttatcac aagttccaag cagtttcaat
2751 acaaacatag gatatgttaa caacttttga taagaatcaa gttaccaact
2801 gttcattgtg agctttgagc tgtatagaag gacaatgtat cccataacct
2851 aatctttaat agtcatcagt cactgggcc gcaccaattt tttcgattcg
2901 catatgtcat atattgcacc gtggcccttt ttattgtaac ttttaatata
2951 ttttcttccc aacttgtgaa tatgattgat gaaccaccat tttgagtaat
3001 aaatgtattt tttgtgg

```

Fig. 11B (sheet 2 of 2)

1	gtaatcaaat	tgtaaaggaa	aaatattaat	agtcagagta	cacataaatg
51	ggtgatcatc	ataatttaac	gggccttccc	ggtacctcca	ccccgccaca
101	gttcaactat	tctcagcccg	gtaccagcac	cggaggcccg	ctttatgggtg
151	gaaaaccttc	tcatggattg	gaagatattc	ctgatgtaga	ggaatatgag
201	aggaacctgc	tcggggctgg	agcaggtttt	aatctgctca	atgtaggaaa
251	tatggctaata	gaatttaaac	caataatcac	attggacacg	aaaccacctc
301	gtgatgccaa	caagtcattg	gcattcaatg	gcggggtgaa	gctaatact
351	ccgaaaactg	aagttcccga	cgagcacaca	ccgatgatgt	caccagtga
401	tacaactaca	aagattctac	aacggagtgg	tattaaaatg	gaaatcccgc
451	catatttgga	tccagacagt	caggatgatg	acccggaaga	tggtgtcaac
501	taccgcatc	cagatttatt	tgacacaaaa	aacacaaata	tgaccgagta
551	cgatttgga	gtgttgaa	ttggaaaacc	agcagtagat	gaagcacgga
601	aaaagatcga	agttcccga	gctagtgcgc	cgccaaacaa	aattgtagaa
651	tatttgatgt	attatagaac	gttaaaagaa	agtgaactca	tacaactgaa
701	tgcgtatcgg	acaaaacgaa	atcgattatc	ggtgaacttg	gtcaaaaaa
751	atattgatcg	agagttcgac	caaaaagctt	gcgagtcctt	ggtgaaaaaa
801	ttgaaggata	agaagaatga	tctccagaac	ctgattgatg	tggttctttc
851	aaaaggtaca	aaatataccg	gttgcatcac	aattccaagg	acacttgatg
901	gccgggtaca	ggtccacgga	agaaaagggt	tccctcacgt	agtctatggc
951	aaactgtgga	ggtttaatga	aatgacaaaa	aacgaaacgc	gtcatgtgga
1001	ccactgcaag	cacgcatttg	aaatgaaaag	tgacatggta	tgctggaatc
1051	cctatcacta	cgaaattgtc	attggaacta	tgattggttg	gcagagggat
1101	catgacaatc	gagatatgcc	gccgccacat	caacgctacc	acactccagg
1151	tcggcaggat	ccagttgacg	atatgagtag	atttatacca	ccagcttcca
1201	ttcgtccgcc	tccgatgaac	atgcacacaa	ggcctcagcc	tatgcctcaa
1251	caattgcctt	cagttggcgc	aacgtttgcc	catcctctcc	cacatcaggc
1301	gccacataac	ccagggggtt	cacatccgta	ctccattgct	ccacagaccc
1351	attaccggtt	gaacatgaac	ccaattccgc	aaatgccgca	aatgccacaa
1401	atgccaccac	ctctccatca	gggatatgga	atgaatgggc	cgagttgctc
1451	ttcagaaaa	aacaatccat	tccacaaaa	tcaccattat	aatgatatta
1501	gccatccaaa	tactattcc	tacgactgtg	gtccgaactt	gtacggggtt
1551	ccaactcctt	atccggattt	tcaccatcct	ttcaatcagc	aaccacacca
1601	gccgccacaa	ctatcacaaa	accatacgtc	ccaacaaggc	agtcataaac
1651	cagggcacca	aggtcaggta	ccgaatgatc	caccaatttc	aagaccagtg
1701	ttacaacat	caacagtcac	cttggacgtg	ttccgtcggg	actgtagaca
1751	gacatttgga	aatcgatttt	ttgaaggaga	aagtgaacaa	tccggcgcaa
1801	taattcggtc	tagtaacaaa	ttcattgaag	aatttgattc	gccgatttgt
1851	ggtgtgacag	ttgttcgacc	gcggatgaca	gacggtgagg	ttttggagaa
1901	catcatgccg	gaagatgcac	catatcatga	catttgcaag	ttcattttga
1951	ggctcacatc	agaaagtgtg	actttctcag	gagagggggc	agaagttagt
2001	gatttgaacg	aaaaatgggg	aacaattgtg	tactatgaga	aaaatttgca
2051	aattggcgag	aaaaaatgtt	cgagaggaaa	tttccacgtg	gatggcggat

Fig. 11C (sheet 1 of 2)

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2101 tcatttgctc tgagaatcgt tacagtctcg gacttgagcc aaatccaatt
2151 agagaaccag tggcgtttaa agttcgtaaa gcaatagtgg atggaattcg
2201 cttttcctac aaaaaagacg ggagtgtttg gcttcaaaac cgcatgaagt
2251 acccggtatt tgtcacttct gggatatctcg acgagcaatc aggaggccta
2301 aagaaggata aagtgcacaa agtttacgga tgtgctgcta tcaaaacggt
2351 tggcttcaac gtttccaaac aaatcatcag agacgcgctt ctttccaagc
2401 aaatggcaac aatgtacttg caaggaaaat tgactccgat gaattatatac
2451 tacgagaaga agactcagga agagctgcga agggaagcaa cacgcaccac
2501 tgattcattg gccaaagtact gttgtgtccg tgtctcgttc tgcaaaggat
2551 ttggagaagc ataccagaa cgcccgtaa ttcatgattg tccagtttgg
2601 attgagttga aaatcaacat tgcctacgat ttcatggatt caatctgcca
2651 gtacataacc aactgcttcg agccgctagg aatggaagat tttgcaaaat
2701 tgggaatcaa cgtcagtgat gactaaatga taactttttt cactcaccct
2751 actagatact gatttagtct tattccaaat catccaacga tatcaaactt
2801 tttcctttga actttgcata ctatgttatc acaagttcca agcagtttca
2851 atacaaacat aggatatgtt aacaactttt gataagaatc aagttaccaa
2901 ctgttcattg tgagctttga gctgtataga aggacaatgt atcccatacc
2951 tcaatcttta atagtcatca gtcactggtc ccgcaccaat tttttcgatt
3001 cgcataatgac atatattgca ccgtggccct ttttattgta acttttaata
3051 tattttcttc ccaacttgtg aatatgattg atgaaccacc attttgagta
3101 ataaatgtat tttttgtgg

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Fig. 11C (sheet 2 of 2)

1	MKLIATSLLV	PDEHTPMMSP	VNTTTKILQR	SGIKMEIPPY	LDPDSQDDDD
51	EDGVNYPDPD	LFDTKNTNMT	EYDLVDLKLK	KPAVDEARKK	IEVPDASAPP
101	NKIVEYLMYY	RTLKESELIQ	LNAYRTKRNR	LSLNLVKNNI	DREFDQKACE
151	SLVKKLKDKK	NDLQNLIDVV	LSKGTKYTGC	ITIPRTL DGR	LQVHGRKGFP
201	HVVYGKLWRF	NEMTKNETRH	VDHCKHAFEM	KSDMVCVNPY	HYEIVIGTMI
251	VGQRDHDNRD	MPPPHQRYHT	PGRQDPVDDM	SRFIPPASIR	PPPMNMHTRP
301	QPMPPQLPSV	GATFAHPLPH	QAPHNPGVSH	PYSIAPQTHY	PLNMNPIPQM
351	PQMPQMPPPL	HQGYGMNGPS	CSSNNNNPFH	QNHHYNDISH	PNHYSYDCGP
401	NLYGFPTPYP	DFHHPFNQQP	HQPPQLSQNH	TSQQGSHQPG	HQGQVPNDPP
451	ISRPVLQPST	VTLDVFRRYC	RQTFGNRFFE	GESEQSGAII	RSSNKFIEEF
501	DSPICGVTVV	RPRMTDGEVL	ENIMPEDAPY	HDICKFILRL	TSESVTFSGE
551	GPEVSDLNEK	WGTIVYYEKN	LQIGEKKCSR	GNFHVDGGFI	CSENRYSLGL
601	EPNPIREPVA	FKVRKAIVDG	IRFSYKKDGS	VWLQNRMKYP	VFVTSGYLDE
651	QSGGLKKDKV	HKVYGCASIK	TFGFNVSKQI	IRDALLSKQM	ATMYLQGKLT
701	PMNYIYEKKT	QEELRREATR	TTDSLAKYCC	VRVSFCKGFG	EAYPERPSIH
751	DCPVWIELKI	NIAYDFMDSI	CQYITNCFEP	LGMEDFAKLG	INVSDD

Fig. 12A

1	MGDHHNLTGL	PGTSIPPQFN	YSQPGTSTGG	PLYGGKPSHG	LEDIPDVEEY
51	ERNLLGAGAG	FNLLNVGNMA	NVPDEHTPMM	SPVNTTTKIL	QRSGIKMEIP
101	PYLDPDSQDD	DPEDGVNYPD	PDLFDTKNTN	MTEYDLDLVK	LGKPAVDEAR
151	KKIEVPDASA	PPNKIVEYLM	YYRTLKESEL	IQLNAYRTKR	NRLSLNLVKN
201	NIDREFDQKA	CESLVKKLKD	KKNLQNLID	VVLSKGTKYT	GCITIPRTLD
251	GRLQVHGRKG	FPHVVGKLW	RFNEMTKNET	RHVDHCKHAF	EMKSDMVCVN
301	PYHYEIVIGT	MIVGQRDHDN	RDMPPPHQRY	HTPGRQDPVD	DMSRFIPPAS
351	IRPPPMNMHT	RPQPMPPQLP	SVGATFAHPL	PHQAPHNPGV	SHPYSIAPQT
401	HYPLNMNPIP	QMPQMPQMPP	PLHQGYGMNG	PSCSSENNNP	FHQNHHYNDI
451	SHPNHYSYDC	GPNLYGFPTP	YPDFHHPFNQ	QPHQPPQLSQ	NHTSQQGSHQ
501	PGHQGQVPND	PPISRPVLQP	STVTLDVFRR	YCRQTFGNRF	FEGESEQSGA
551	IIRSSNKFIE	EFDSPICGVT	VVRPRMTDGE	VLENIMPEDA	PYHDICKFIL
601	RLTSESVTFS	GEGPEVSDLN	EKWGTIVYYE	KNLQIGEKKC	SRGNFHVDDG
651	FICSENRYSL	GLEPNPIREP	VAFKVRKAIV	DGIRFSYKKD	GSVWLQNRMK
701	YPVFVTSGYL	DEQSGGLKGD	KVHKVYGCAS	IKTFGFNVSK	QIIRDALLSK
751	QMATMYLQGK	LTPMNYIYEK	KTQEELRREA	TRTTDSLAKY	CCVRVSFCKG
801	FGEAYPERPS	IHDCPVWIEL	KINIAYDFMD	SICQYITNCF	EPLGMEDFAK
851	LGINVSDD				

Fig. 12B

1	MGDHHNLTGL	PGTSIPPQFN	YSQPGTSTGG	PLYGGKPSHG	LEDIPDVEEY
51	ERNLLGAGAG	FNLLNVGNMA	NEFKPIITLD	TKPPRDANKS	LAFNGGLKLI
101	TPKTEVPDEH	TPMMSPVNTT	TKILQRSGIK	MEIPPYLDPD	SQDDDPEDGV
151	NYPDPDLFDT	KNTNMTEYDL	DVLKLGKPAV	DEARKKIEVP	DASAPPNKIV
201	EYLMYYRTLK	ESELIQLNAY	RTKRNRLSLN	LVKNNIDREF	DQKACESLVK
251	KLKDKKNDLQ	NLIDVVL SKG	TKYTGCTIP	RTLDGRLQVH	GRKGFPHVYV
301	GKLWRFNEMT	KNETRHDVHC	KHAFEMKSDM	VCVNPYHYEI	VIGTMIVGQR
351	DHDNRDMPPP	HQRYHTPGRQ	DPVDDMSRFI	PPASIRPPPM	NMHTRPQMP
401	QQLPSVGATF	AHPLPHQAPH	NPGVSHPSYI	APQTHYPLNM	NPIPQMPQMP
451	QMPPLHQGY	GMNGPSCSSE	NNNPFHQNH	YNDISHPNHY	SYDCGPNLYG
501	FPTPYPDFHH	PFNQPPHQPP	QLSQNHTSQQ	GSHQPGHQGQ	VPNDPPISRP
551	VLQPSTVTLD	VFRRYCRQTF	GNRFFEGESE	QSGAIRSSN	KFIEEFDSP
601	CGVTVVRPRM	TDGEVLENIM	PEDAPYHDIC	KFILRLTSES	VTFSGEGPEV
651	SDLNEKWGTI	VYYEKNLQIG	EKKCSRGNFH	VDGGFICSEN	RYSLGLEPNP
701	IREPVAFKVR	KAIVDGIRFS	YKKGDSVWLQ	NRMKYPVFVT	SGYLDEQSGG
751	LKKDKVHKVY	GCASIKTFGF	NVSKQIIRDA	LLSKQMATMY	LQGLTPMNY
801	IYEKKTQEEL	RREATRTTDS	LAKYCCVRVS	FCKGFGEAYP	ERPSIHDCPV
851	WIELKINIAY	DFMDSICQYI	TNCFEPLGME	DFAKLGINVS	DD

Fig. 12C

tgatctttcaagccgaagcaatcaagacctcaaagccaatcaactctactcactttttcttcagaaccttaactttttgtg
 tcactttccccaaaaaccgttcaagctgctgccttactctcatccctcctcttactccttctttctcgtccgtacta
 ctgtatcttctggacatctacctgtatacacaccagtggccagtcacatgccattacaatttcatcaattgacacttctt
 caacaacaaccgccgtcctcattcactcccgtattcttctcatcctcaacatcgtcgtctttggctgaaattcccgaaga
 cgttatgatggagatgctggtagatcagggaaactgatgcacgtcatccgcctccacgtccacctcatctgtttcgagat
 tcggagcggacacgttcatgaatacacccgatgatgtgatgatgaatgatgatggaaccgattcctcgtgatcgggtgc
 aatacgtggccaatgcgtaggccgcaactcgaaccaccactcaactcgagtcctcatttcatgaacaaattcctgaaga
 agatgctgacctatacgggagcaatgagcaatgtggacagctcggcggagcatcttcaaacgggtcgacagcaatgcttc
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Fig. 13A

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Fig. 13B

MMEMLVDQGTDASSSASTSTSSVSRFGADTFMNTPDVMMNDDMEPIPRDR
 CNTWPMRRPQLEPPLNSSPIIHEQIPEEDADLYGSNEQCGQLGGASSNGST
 AMLHTPDGNSNSHQTSFSPDFRMSESPDDTVSGKKTTRRNAWGNMSYAELI
 TTAIMASPEKRLTLAQVYEWVQNVYPYFRDKGDSNSSAGWKNSIRHNLSLH
 SRFMRIQNEGAGKSSWWVINPDAKPGMNPRRTRERSNTIETTTKAQLEKSR
 RGAKKRIKERALMGSLHSTLNGNSIAGSIQTISHDLYDDDSMQGAFDNVPSS
 SFRPRTQSNLSIPGSSSRVSPAIGSDIYDDLEFPSWVGESVPAIPSDIVDR
 TDQMRIDATTHIGGVQIKQESKPIKTEPIAPPPSYHELNSVRGSCAQNP LL
 RNPIVPSTNFKPMPLPGAYGNYQNGGITPINWLSTSNSSPLPGIQSCGIVA
 AQHTVASSALPIDLENLTLPDQPLMDTMDVDALIRHEL SQAGGQHIHFDL

Fig. 14A

MQQYIYQESSATIPHHHLNQHNPNYPHMPHHQLPHMQQLPQPLLNLNMTT
 LTSSGSSVASSIGGGAQCSPCASGSSTAATNSSQQQQTVGQMLAASVPCSS
 SGM TLGMSLNL SQGGGPMPAKKKRCRKKPTDQLAQKKPNPWGEESYSDIIA
 KALESAPDGRLKLNEIYQWFS DNIPYFGERSSP EEAAGWKNSIRHNLSLHS
 RFMRIQNEGAGKSSWWVINPDAKPGMNPRRTRERSNTIETTTKAQLEKSRR
 GAKKRIKERALMGSLHSTLNGNSIAGSIQTISHDLYDDDSMQGAFDNVPSS
 FRPRTQSNLSIPGSSSRVSPAIGSDIYDDLEFPSWVGESVPAIPSDIVDRT
 DQMRIDATTHIGGVQIKQESKPIKTEPIAPPPSYHELNSVRGSCAQNP LLR
 NP IVPSTNFKPMPLPGAYGNYQNGGITPINWLSTSNSSPLPGIQSCGIVAA
 QHTVASSALPIDLENLTLPDQPLMDTMDVDALIRHEL SQAGGQHIHFDL

Fig. 14B

1	cggaagccat	ggagctcgag	atctgattgc	tggacacgga	cggaactccg	acgtatctcg
61	cagatgcatg	ttaacatttt	acatccacaa	ctgcaaacga	tggtcgagca	gtggcaaatg
121	cgagaacgcc	catcgctgga	gaccgagaat	ggcaaaggat	cgctgctcct	ggaaaatgaa
181	ggtgtcgag	atatcatcac	tatgtgtcca	ttcggagaag	ttattagtgt	agtatttccg
241	tggtttcttg	caaatgtgag	aacatcgcta	gaaatcaagc	tatcagattt	caaacatcaa
301	cttttcgaat	tgattgctcc	gatgaagtgg	ggaacatatt	ccgtaaagcc	acaggattat
361	gtgttcagac	agttgaataa	tttcggcgaa	attgaagtta	tatttaacga	cgatcaaccc
421	ctgtcgaaat	tagagctcca	cggcactttc	ccaatgcttt	ttctctacca	acctgatgga
481	ataaacaggg	ataaagaatt	aatgagtgat	ataagtcatt	gtctaggata	ctcactggat
541	aaactggaag	agagcctcga	tgaggaactc	cgtcaatttc	gtgcttctct	ctgggctcgt
601	acgaagaaaa	cgtgcttgac	acgtggactt	gagggtacca	gtcactacgc	gttccccgaa
661	gaacagtact	tgtgtgttgg	tgaatcgtgc	ccgaaagatt	tggaatcaaa	agtcaaggct
721	gccaaagctga	gttatcagat	gttttgagaa	aaacgtaaag	cggaaatcaa	tggagtttgc
781	gagaaaaatga	tgaagattca	aattgaattc	aatccgaacg	aaactccgaa	atctctgctt
841	cacacgtttc	tctacgaaat	gcgaaaattg	gatgtatacg	ataccgatga	tcctgcagat
901	gaaggatggt	ttcttcaatt	ggctggacgt	accacgtttg	ttacaaatcc	agatgtcaaa
961	cttacgtctt	atgatggtgt	ccgttcggaa	ctggaaagct	atcgatgcc	tggattcgtt
1021	gttcgccgac	aatcactagt	cctcaaagac	tattgtcgcc	caaaaccact	ctacgaacca
1081	cattatgtga	gagcacacga	acgaaaactt	gctctagacg	tgctcagcgt	gtctatagat
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1381	aaatggaata	aggaaatgta	cacttttgat	ctatacatga	aggatatgcc	accatctgca
1441	gtactcagca	ttcgtgtttt	gtacggaaaa	gtgaaattaa	aaagtgaaga	attcgaagtt
1501	ggttgggtaa	atatgtccct	aaccgattgg	agagatgaac	tacgacaagg	acaattttta
1561	ttccatctgt	gggctcctga	accgactgcc	aatcgtagta	ggatcggaga	aaatggagca
1621	aggataggca	ccaacgcagc	ggttacaatt	gaaatctcaa	gttatgggtg	tagagttcga
1681	atgccgagtc	aaggacaata	cacatatctc	gtcaagcacc	gaagtacttg	gacggaaact
1741	ttgaatatta	tgggtgatga	ctatgagtcg	tgtatcagag	atccaggata	taagaagctt
1801	cagatgcttg	tcaagaagca	tgaatctgga	attgtattag	aggaagatga	acaacgtcat
1861	gtctggatgt	ggaggagata	cattcaaaaag	caggagcctg	atttgtcat	tgtgctctcc
1921	gaactcgcat	ttgtgtggac	tgatcgtgag	aacttttccg	agctctatgt	gatgcttgaa
1981	aaatggaaac	cgccgagtg	ggcagccgcg	ttgactttgc	ttggaaaacg	ttgcacggat
2041	cgtgtgattc	gaaagtttgc	agtggagaag	ttgaatgagc	agctgagccc	ggtcacattc
2101	catcttttca	tattgcctct	catacaggcg	ttgaagtacg	aaccgcgtgc	tcaatcggaa
2161	gttggaatga	tgctcttgac	tagagctctc	tgcgattatc	gaattggaca	tcgacttttc
2221	tggtgctcc	gtgcagagat	tgctcgtttg	agagattgtg	atctgaaaag	tgaagaatat
2281	cgccgtatct	cacttctgat	ggaagcttac	ctccgtggaa	atgaagagca	catcaagatc
2341	atcaccggac	aagttgacat	ggttgatgag	ctcacacgaa	tcagcactct	tgtcaaagga
2401	atgccaaaag	atgttgctac	gatgaaactg	cgtgacgagc	ttcgatcgat	tagtcataaa
2461	atggaaaata	tggattctcc	actggatcct	gtgtacaaac	tgggtgaaat	gataatcgac
2521	aaagccatcg	tcctaggaag	tgcaaaacgt	ccgttaatgc	ttcactggaa	gaacaaaaat
2581	ccaaagagtg	acctgcacct	tccgttctgt	gcaatgatct	tcaagaatgg	agacgatctt
2641	cgccaggaca	tgcttgttct	tcaagttctc	gaagttatgg	ataacatctg	gaaggctgca

Fig. 15 (sheet 1 of 2)

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2701 aacattgatt gctgtttgaa cccgtacgca gttcttccaa tgggagaaat gattggaatt
2761 attgaagttg tgcctaattg taaaacaata ttcgagattc aagttggaac aggattcatg
2821 aatacagcag ttcggagtat tgatccttcg tttatgaata agtggattcg gaaacaatgc
2881 ggaattgaag atgaaaagaa gaaaagcaaa aaggactcta cgaaaaatcc catcgaaaag
2941 aagattgata atactcaagc catgaagaaa tattttgaaa gtgtcgatcg attcctatac
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3361 gatcatttga agaaaaccct cttctgcaat ggagaaagca aagaagaagc gagaaagttt
3421 ttcgctggaa tctacgaaga agccttcaat ggatcatggt ctaccaaacc gaattggctc
3481 ttccacgcag tcaaactact ctga

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Fig. 15 (sheet 2 of 2)

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1 RKPWSSRSDC WTRTELRRIS QMHVNILHPQ LQTMVEQWQM RERPSLETEN GKGSLLLENE
61 GVADIITMCP FGEVISVFP WFLANVRTSL EIKLSDFKHQ LFELIAPMKW GTYSVKPQDY
121 VFRQLNNGFE IEVIFNDDQP LSKLELHGTF PMLFLYQPDG INRDKELMSD ISHCLGYSLD
181 KLEESLDEEL RQFRASLWAR TKKTCLTRGL EGTSHYAFPE EQYLCVGESC PKDLESKVKA
241 AKLSYQMFWR KRKAEINGVC EKMMKIQIEF NPNETPKSL LHTFLYEMRKL DVYDTDDPAD
301 EGWFLQLAGR TTFVTNPDKV LTSYDGVRS ELESYRCPGFV VRRQSLVLKD YCRPKPLYEP
361 HYVRAHERKL ALDVLSVSD STPKQSKNSD MVMTDFRPTA SLKQVSLWDL DANLMIRPVN
421 ISGFDFPADV DMYVRIEFSV YVGTTLT LASK STTKVNAQFA KWNKEMYTFD LYMKDMPPSA
481 VLSIRVLYGK VKLKSEEFV GWVNMSLTDW RDELROGQFL FHLWAPEPTA NRSRIGENGA
541 RIGTNAAVTI EISSYGGRVR MPSQGQYTYL VKHRSTWTET LNIMGDDYES CIRDPGYKKL
601 QMLVKKHESG IVLEEDEQRH VWMWRRYIQK QEPDLLIVLS ELAFVWTDRE NFESELYVME
661 KWKPPSVAAA LTLLGKRCTD RVIRKFAVEK LNEQLSPVTF HLFILPLIQA LKYEPRQSE
721 VGMMLLTRAL CDYRIGHRLF WLLRAEIARL RDCDLKSEY RRISLLMEAY LRGNEEHIKI
781 ITRQVDMVDE LTRISTLVKG MPKDVATMKL RDELRSISHK MENMDSPLDP VYKLGEMIID
841 KAIVLGSKR PLMLHWKNKN PKSDLHLPFC AMIFKNGDDL RQDMLVLQVL EVMDNIWKAA
901 NIDCCLNPYA VLPMGEMIGI IEVVPNCKTI FEIQVGTGFM NTAVRSIDPS FMNKWIRKQC
961 GIEDEKKKSK KDSTKNPIEK KIDNTQAMKK YFESVDRFLY SCVGYSVATY IMGIDRHS D
1021 NLMLTEDGKY VHIDFGHILG HGKTKLGIQR DRQPFILTEH FMTVIRSGKS VDGNSHELQK
1081 FKTLCEAYE VMWNNRDLFV SLFTLMLGME LPELSTKADL DHLKKTLCFN GESKEEARKF
1141 FAGIYEEAFN GSWSTKTNLW FHAVKHY

```

Fig. 16

CONVERGENT TGF- β AND INSULIN SIGNALING ACTIVATE GLUCOSE-BASED METABOLISM GENES

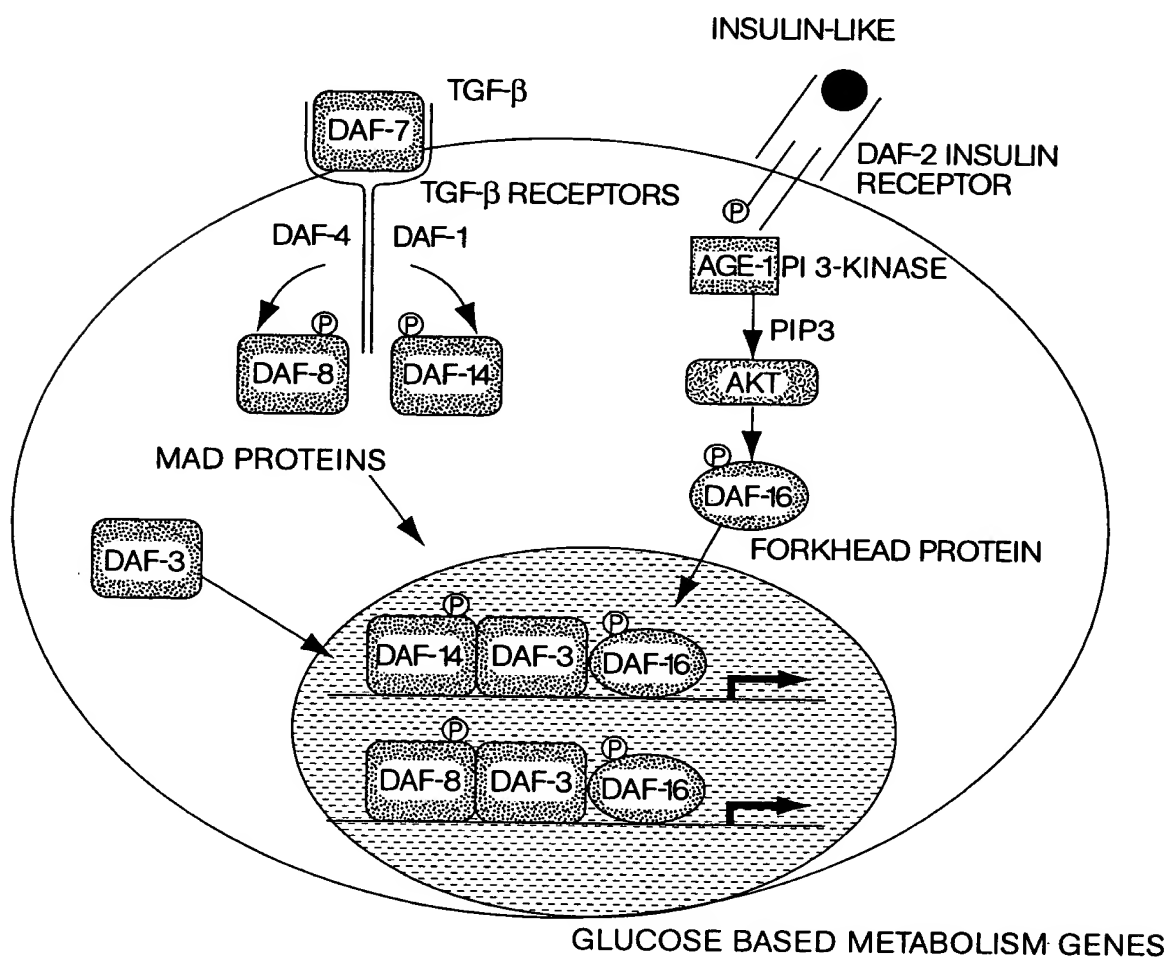


Fig. 17

IN PHEROMONE, NO TGF β OR INSULIN-LIKE SIGNALS
CAUSES REPRESSION OF ANABOLIC GENES

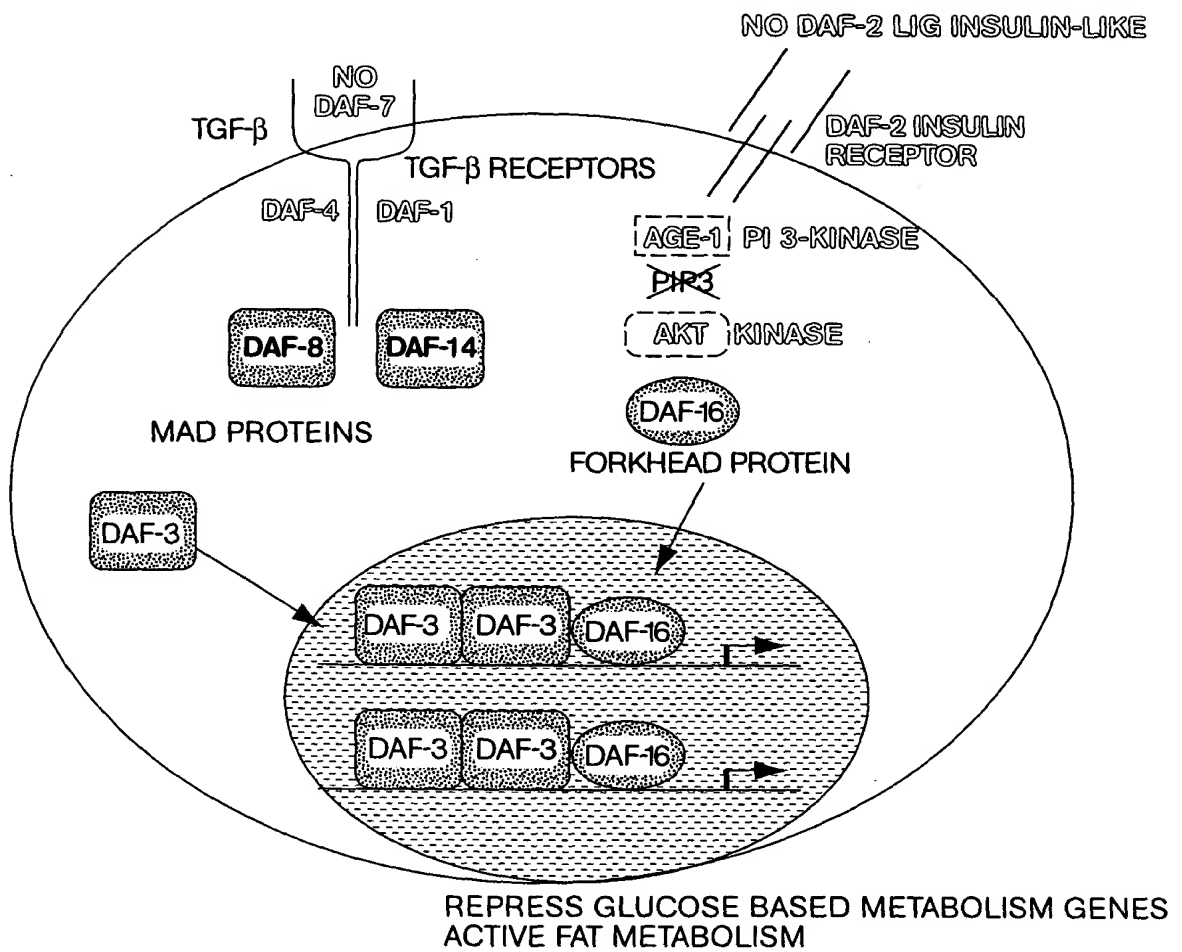
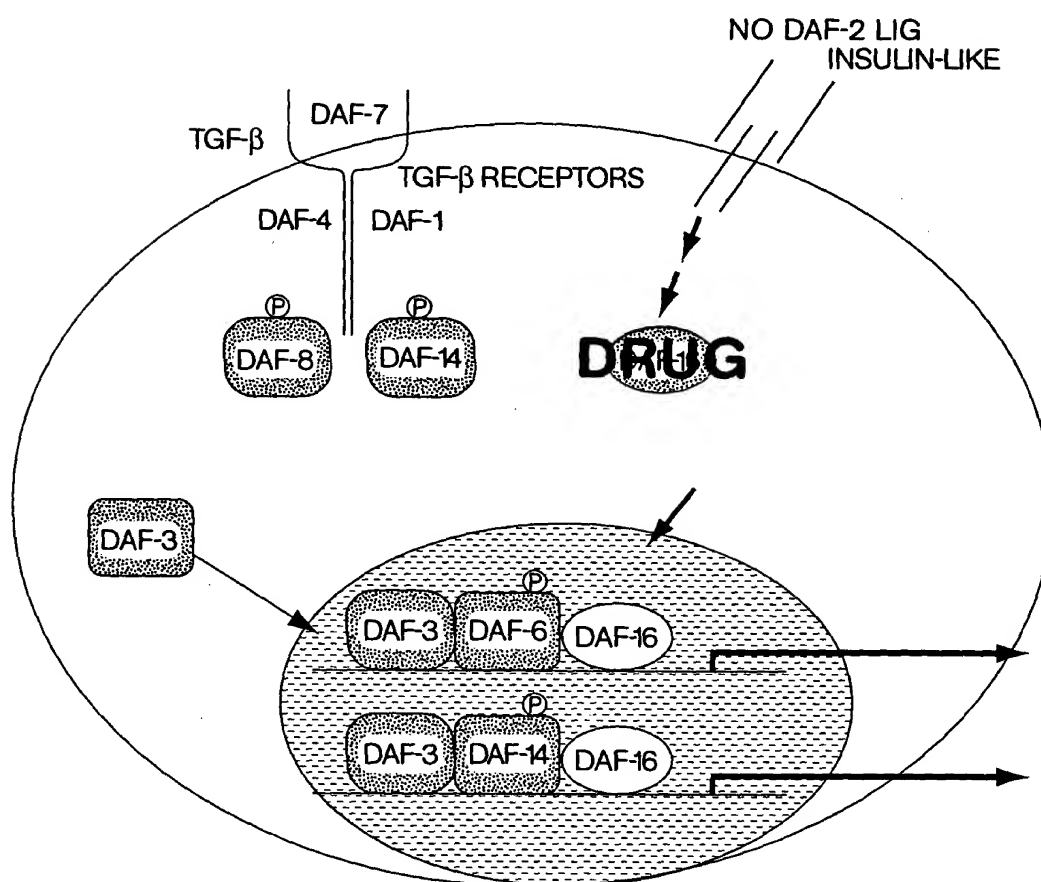


Fig. 18

DRUGS THAT INHIBIT DAF-16 OR DAF-3
(OR PROTEINS IN THE PATHWAY)
CAN BE DISCOVERED USING REPORTER GENES
BEARING THEIR COGNATE BINDING SITES



DRUG CAUSES A DECREASE IN DAF-16 ACTIVITY, ACTIVATING
THE REPORTER GENE LIKE A DAF-16 MUTANT.
THIS BYPASSES THE NEED FOR INSULIN

Fig. 19

**DRUGS THAT INHIBIT DAF-3 WILL CURE
THE DIABETES CAUSED BY A LACK OF DAF-7**

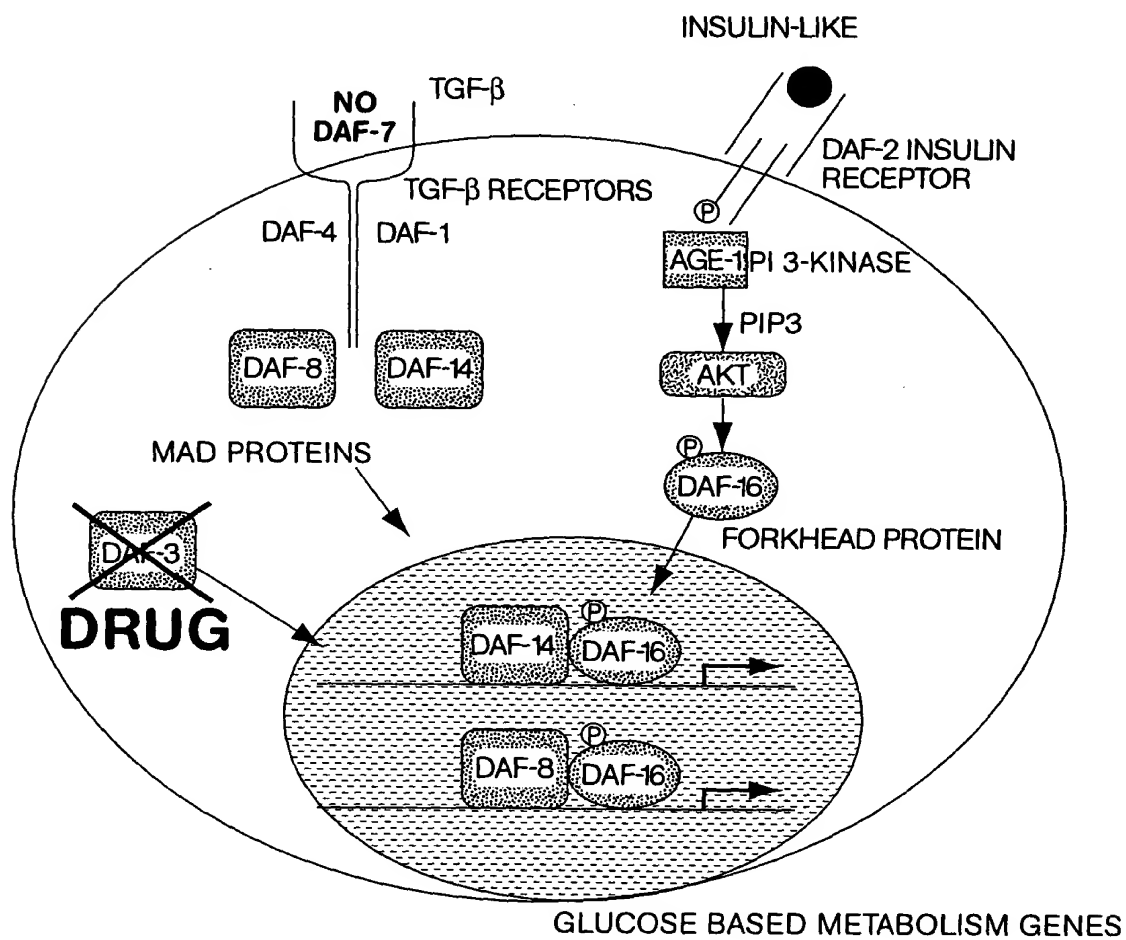


Fig. 20

[illegible]

Fig. 21A (sheet 1 of 3)

Hnf3a	SLITMAIQRA	PSKMLTLSEI	YQWIMDLFPY	YRQNRQ...	..WQNSIRHS	LSLND	227
Hnf3g	SLITMAIQQA	PCKVLTLSL	YQWIMDLFPY	YRDNQQR...	..WQNSIRHS	LSLND	171
D16123a467891011	ELITTAJMAS	PEKRLTLAQ	YEWVQNVVPY	FRDKGDSNSS	AGWKNISIRHN	LSLHS	205
D1612567891011	DIHAKALES	PDGRKLNEL	YQWFSNIPY	FGERSPEEA	AGWKNISIRHN	LSLHS	330
Afx	EELISQALES	PEKRLTLAQ	YEWVVRTVPY	FKDKGDSNSS	AGWKNISIRHN	LSLHS	158
Fkhr	DLITKAIESS	AEKRLTLQI	YEWVVKSVPY	FKDKGDSNSS	AGWKNISIRHN	LSLHS	221
Consensus	-LIT-AI-A	P-KRLTL-I	Y-W-----PY	F-D-----	AGWKNISIRHN	LSLHS	330
Hnf3a	CFVKVARSPD	KPGKGSMTL	HPDSG.....NM	FENGCYLRRQ	KRFKC	269
Hnf3g	CFVKVARSPD	KPGKGSMTL	HPSSG.....NM	FENGCYLRRQ	KRFKL	213
D16123a467891011	RFMRQON..E	GAGKSSWV	NPD..KPGMN	PRRTRETSNT	IETTTKAQLE	KSRRG	257
D1612567891011	RFMRQON..E	GAGKSSWV	NPD..KPGMN	PRRTRETSNT	IETTTKAQLE	KSRRG	382
Afx	KFIKVHN..E	ATGKSSWML	NPEGKSGKA	PRR...RAAS	MDSSSKLLRG	RSKAP	208
Fkhr	KFIKVON..E	GTGKSSWML	NPEGKSGKS	PRR...RAAS	MDNNSKFAKS	RSRAA	271
Consensus	-F-V-N-E	--GKSSW-L	NP--GK-G--	PRR--R-N-	-E--K----	KS----	385
Hnf3a	EKQPGAG...	GGGSGSGGS	GAKGPESRK	DPSGASNP	DSPLHRGVHG	KTGQL	321
Hnf3g	EKQVKKG...	GGGASTTRNC	TGSAASTTTP	AATVTSP...	QCAFDDNVPS	FRPRT	248
D16123a467891011	AKKRIKERAL	MGSHTSLNC	NSIAGSIQTI	SHDLYDDDSM	QCAFDDNVPS	FRPRT	312
D1612567891011	AKKRIKERAL	MGSHTSLNC	NSIAGSIQTI	SHDLYDDDSM	QCAFDDNVPS	FRPRT	437
Afx	KKKP.....	SVLPAPPEG	ATPTSPVGHF	AKWSGSPCSR	NREEADMWTT	FRPRS	256
Fkhr	KKKA.....	S.LQSGQEC	AG.DSPGSQF	SKWPAFPGSH	SNDFFDNWST	FRPRT	317
Consensus	-KK-----	--L-----G	-----	-----S-S-	-----	FRPR-	440
Hnf3a	EGAPAPGPAA	SPQTLDHSGA	TATGGASELK	TPASSSTAPPI	SSGPGALASV	PASHP	376
Hnf3g	.OPPPPAPEP	EAQGGEDVGA	LDCGS.....	.PASSSTP...	PAIGS.....	278
D16123a467891011	QSNLS.....	IPGSS.SRVS	PAIGS.....	331
D1612567891011	QSNLS.....	IPGSS.SRVS	PAIGS.....	456
Afx	SSNASSVSTR	LSPLRPESEV	LAEE.....	IPASV.SSYA	GGVPPPTLN..	..EGL	300
Fkhr	SSNASTISGR	LSPIMTQDD	LGEGDVHSMV	YPPSA.AKMA	STLPSLSEIS	NPENM	371
Consensus	-SN-S-----	-----	-----	-P-SS-----	-----	-----	495
Hnf3a	AHGLAPHESQ	LHLKGDPHYS	FNHFFSINNLL	MSS.SEQCHK	LDPKAYEQAL	QYSPY	430
Hnf3g	..YFTGLELP	GDLKLDAPYN	FNHFFSINNLL	MSEQTPAPPK	LD.....V	GFGGY	324
D16123a467891011	.DIYDDLEF.	..PSWVGESV	PAIP.....	351
D1612567891011	.DIYDDLEF.	..PSWVGESV	PAIP.....	476
Afx	E.LLDGLNLT	SSHSLLSRSG	LSG.....	FSLQHPGVTC	PLHTY	337
Fkhr	ENLLDNLL	SSPTSLTVST	QSSEGTMMQ	TPCYSFAPPN	TSINSPSPNY	QKTYT	426
Consensus	-----D-LE-	-----S-	-----P-----	-----	-----	-----	550

Fig. 21A (sheet 2 of 3)

Hnf3a	GSTLPASLPL	GSASVTRSP	IEPSALEPAY	YQGVYSRPVL	NTS	473		
Hnf3g	GAE	GGEPGVY	YQGLYSRSL	NAS	347		
D16123a467891011	RTDQMRIDAT	THIGGVQ	IKQESKPIK	TEPIAPP	PPSY HELNS	397		
D1612567891011	RTDQMRIDAT	THIGGVQ	IKQESKPIK	TEPIAPP	PPSY HELNS	522		
Afx	SSSLFSP	AE	GPISSGEGCF	SSSQALEAL	TS	DTPPPAD VLMTQ	381	
Fkhr	GQSSMSPLPQ	MPIQTLQDNK	SSYGGMSQYN	CAPGLLKE	TS	DSPPH	N DIMTP	479	
Consensus	-----S-----	-----	-----GG-----	-----S-----	-----P-----	-----P-----	605		
Hnf3a	473		
Hnf3g	347		
D16123a467891011	VRGSCA	QNP	AYGNYQNGGI	TPINWLSTSN	SSPLP	450	
D1612567891011	VRGSCA	QNP	AYGNYQNGGI	TPINWLSTSN	SSPLP	575	
Afx	VDPILS	QAPT	LL	LGG	LPSS	SKLA	PKPLE	416
Fkhr	VDPGVA	QPN	RV	QNVMMG	PNSVMSTYGS	QASH	NKMM	NPSSHTPHGH	532
Consensus	V-----Q-----	-----P-----	-----	-----	-----	-----	-----	660	
Hnf3a	473		
Hnf3g	347		
D16123a467891011	GIQSCGIVAA	QHTVASSSAL	PIDLENLTLP	DOPLMDTM	488		
D1612567891011	GIQSCGIVAA	QHTVASSSAL	PIDLENLTLP	DOPLMDTM	613		
Afx	ARGPSS	LVPT	LSMIA	PPVPM	AS	458		
Fkhr	AVNGRPLPHT	VSTMPHTSGM	NRLTQVKTPV	QVPLPHPMQM	PVLTPTTEAA	S	SCNGY	587	
Consensus	-----	-----	-----	-----P-----	-----	-----	715		
Hnf3a	473		
Hnf3g	347		
D16123a467891011	510		
D1612567891011	635		
Afx	QDR	MPQDL	LDLDMY	MENLECDMDN	IS	501		
Fkhr	GRMGLLHQEK	LPSDLD	GMF	IERLDCD	MES	IERNDLMDGD	641		
Consensus	-----	-----	-----	-----D-----	-----	-----P-----	770		
Hnf3a	473		
Hnf3g	347		
D16123a467891011	510		
D1612567891011	635		
Afx	501		
Fkhr	PHSVKTTTHS	WVSG	655		
Consensus	-----	-----	-----	-----	-----	-----	784		

Fig 21A (sheet 2 of 2)

Fig. 21A (sheet 3 of 3)

FOA210" ESE41360

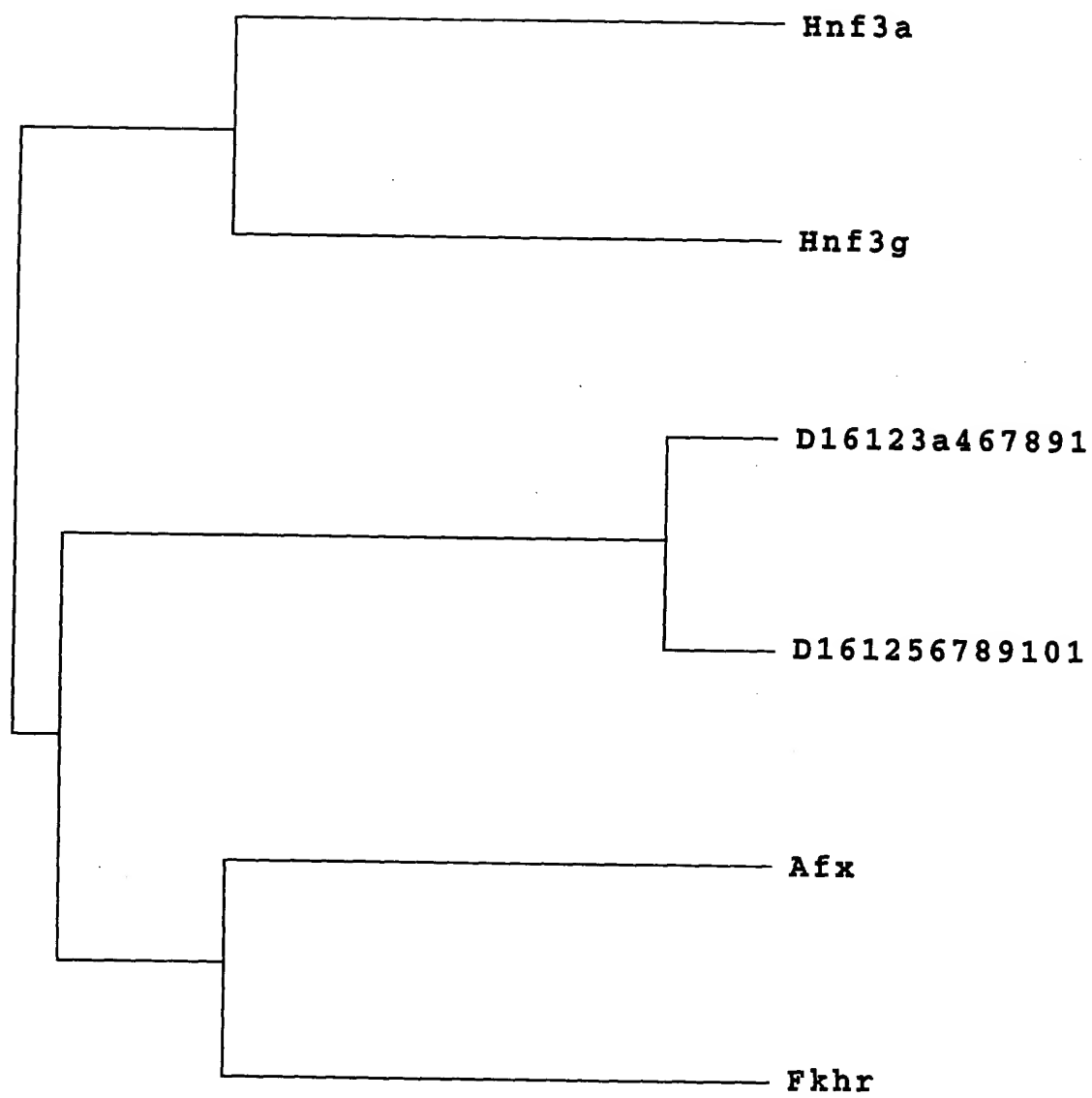


Fig. 21B

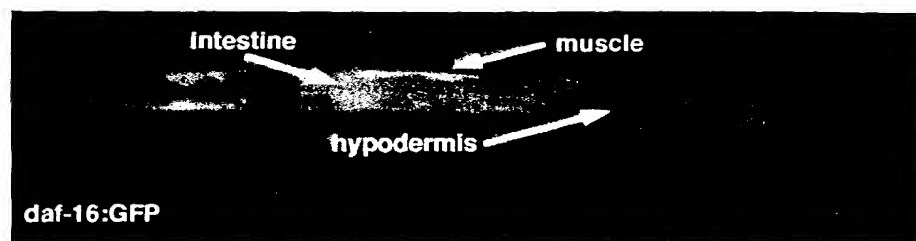


Fig. 22

INJECTION OF OF DAF-7 BYPASSES OBESITY-INDUCED DEFECTS IN INSULIN-REGULATION OF METABOLISM

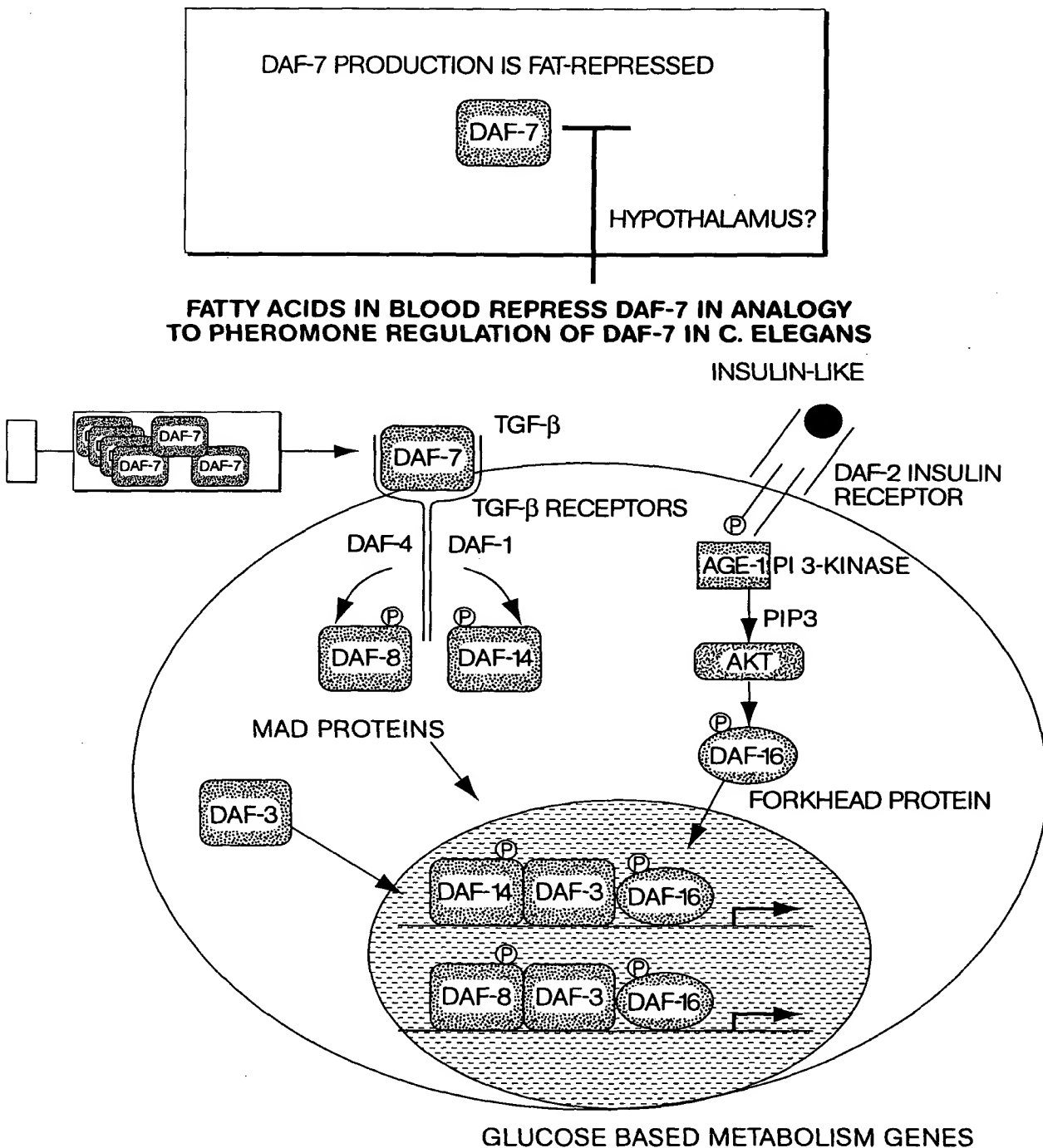


Fig. 23

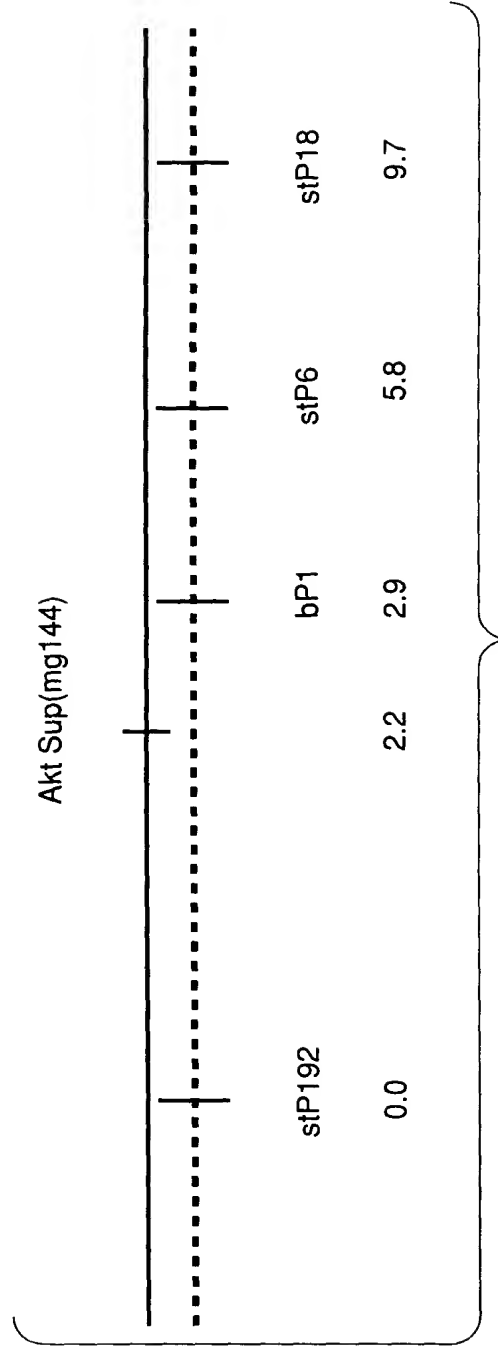


Fig. 24

Comparison of the human AKT protein sequence to the cosmid sequence C12D8, located in the genetic interval where sup(mg144) maps. Numbering in the AKT protein sequence by amino acid residues, and in the cosmid sequence by nucleotide position.

Score = 450 (207.4 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 79/121 (65%), Positives = 97/121 (80%), Frame = +1

Query: 319 EVLEDNDYGRAVDWWGLGVVYEMMCGRLPFYNQDHEKLFELILMEEIRFPRTLGPPEAKS 378
+VL+D+DYGR VDWVG+GVVYEMMCGRLPFY++DH KLFELI+ ++RFP L EA++
Sbjct: 33685 QVLDDHDYGRCDWWGVGVVYEMMCGRLPFYSKDHNLKLFELIMAGDLRFPKLSQEART 33864

Query: 379 LLSGLLKKDPTQRLGGGSEDAKEIMQHRFFANIVWQDVYEKKLSPPFKPQVTSETDTRYFD 439
LL+GLL KDPTQRLGGG EDA EI + FF + W+ Y K++ PP+KP V SETDT YFD
Sbjct: 33865 LLTGLLVKDPTQRLGGGPEDALEICRADFFRTVDWEATYRKEIEPPYKPNVQSETDTSYFD 34047

Score = 256 (118.0 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 48/66 (72%), Positives = 59/66 (89%), Frame = +1

Query: 146 TMNEFEYLKLLGKGTFGKVILVKEKATGRYYAMKILKKEVIVAKDEVAHTLTENRVLQNS 205
TM +F++LK+LGKGTFGKVIL KEK T + YA+KILKK+VI+A++EVAHTLTENRVLQ
Sbjct: 32314 TMEDFDPLKVLGKGTFGKVILCKEKRTQKLYAIKILKRDVITAREEVAHTLTENRVLQRC 32493

Query: 206 RHPFLT 211
+HPFLT
Sbjct: 32494 KHPFLT 32511

Score = 190 (87.6 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 36/45 (80%), Positives = 37/45 (82%), Frame = +2

Query: 276 KLENLMLDKDGHKIDTDFGLCKEGIKDGATMKTFCGTPEYLAPEV 320
KLENL+LDKDGHIKI DFGLCKE I G TFCGTPEYLAPEV
Sbjct: 33509 KLENLLLDKDGHIKIADDFGLCKEEISFGDKTSTFCGTPEYLAPEV 33643

Score = 188 (86.7 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 37/57 (64%), Positives = 42/57 (73%), Frame = +3

Query: 209 FLTALKYSFQTHDRLCFVMEYANGGELFFHLSRERVFSEDRARFYGAIEVSALDYLIH 265
+ LKYSFQ LCFVM++ANGGELF H+ + FSE RARFYGAIEV AL YLIH
Sbjct: 32667 YFQELKYSFQEQHYLCFVMQFANGGELFTHVRKCGTFSEPRARFYGAIEVLALGYLIH 32837

Score = 166 (76.5 bits), Expect = 5.2e-165, Sum P(7) = 5.2e-165
Identities = 29/59 (49%), Positives = 42/59 (71%), Frame = +1

Query: 53 NNFSVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHVETPEEREWEATAIQTVADGLK 111
+ F++ Q M E+PRPN F++RCLQWTTVIERTF+ E+ E R+ W AI++++ K
Sbjct: 31846 STFAIFYFQTMLEKPRPNMFMVRCLQWTTVIERTFYAESAEVRQRWIHAIESISKKYK 32022

Score = 134 (61.8 bits), Expect = 5.2e-167, Sum P(8) = 5.2e-167
Identities = 24/33 (72%), Positives = 30/33 (90%), Frame = +3

Query: 210 LTALKYSFQTHDRLCFVMEYANGGELFFHLSRE 242
L LKYSFQT+DRLCFVME+A GG+L++HL+RE
Sbjct: 33156 LQELKYSFQTNDRLCFVMEFAIGGDLYYHLNRE 33254

Fig. 25



Fig. 26A

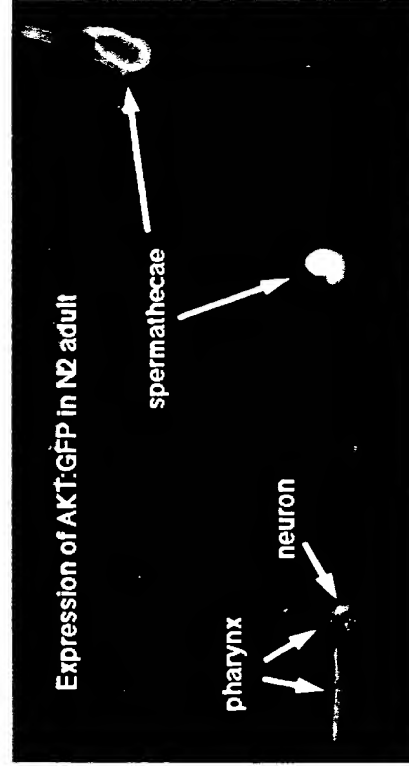


Fig. 26B

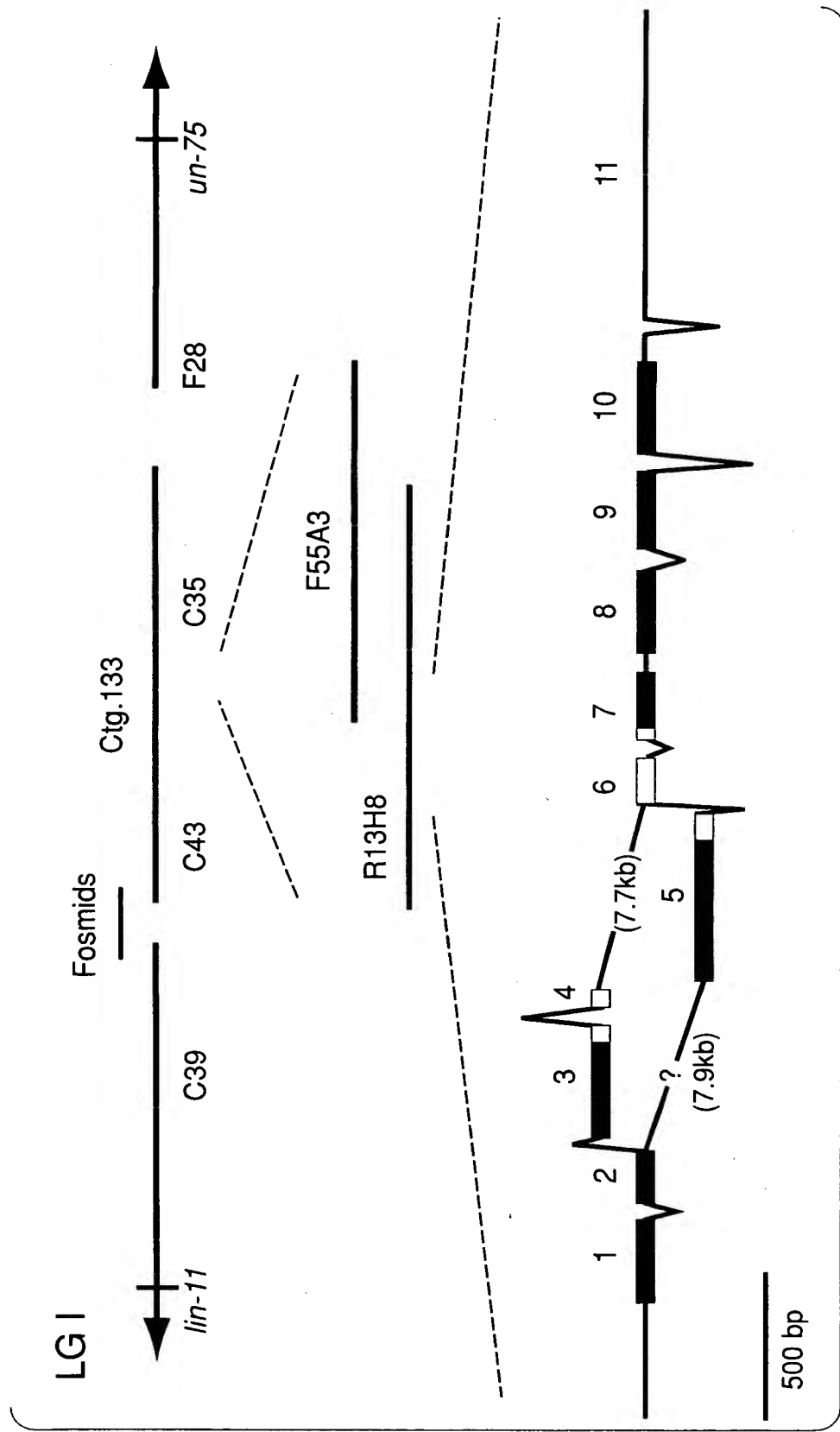


Fig. 27